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REVIEW

Lepidium meyenii (Maca) in male reproduction

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ABSTRACT

Lepidium meyenii (Maca) is an edible root plant that grows in the Andean region of Peru. For centuries, the plant has been used as a dietary supplement for its nutritional and therapeutic properties. Maca are rich in high value nutritional elements and secondary metabolites (macaridine, macamides and glucosinolates) with high biological activity. Several studies demonstrated various biological effects of Maca mainly in the field of fertility. The aim of this review is to summarize the state of knowledge on the properties of Maca on male reproduction. Literature data was performed in PubMed with researches published from 2000 to 2019. The research showed results related to the effects of Maca on the quality and quantity of the semen, sexual behaviour and disorders of the male genital tract. Despite the numerous studies carried out on different animal species, further research is needed to clarify the mechanisms of action of Maca.

Lepidium meyenii (Maca) is an edible root plant that grows in the Andean region of Peru. For centuries, the plant has been used as a dietary supplement for its nutritional and therapeutic properties. Maca are rich in high value nutritional elements and secondary metabolites (macaridine, macamides and glucosinolates) with high biological activity. Several studies demonstrated various biological effects of Maca mainly in the field of fertility. The aim of this review is to summarize the state of knowledge on the properties of Maca on male reproduction. Literature data was performed in PubMed with researches published from 2000 to 2019. The research showed results related to the effects of Maca on the quality and quantity of the semen, sexual behaviour and disorders of the male genital tract. Despite the numerous studies carried out on different animal species, further research is needed to clarify the mechanisms of action of Maca.

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1. Introduction

Lepidium meyenii, known as Maca, is an edible root plant, belonging to the Brassicaceae family, that grows in the Andean region of Peru between 3000–4000 m above sea level. Since 1,300–2,000 years ago, the Andean population appreciates the qualities of Maca as a dietary supplement for its nutritional and therapeutic properties. The interests in the use of this plant are due to its positive effect on female reproductive functions, osteoporosis, depression, anxiety, memory, energy, male sexual

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functions, spermatogenesis and benign prostatic hyperplasia of different species of mammals, including humans (Gonzales et al. 2007; Brooks et al. 2008; Clément et al. 2010a, 2012).

Tello et al. (1992) describe 13 phenotypes of Maca characterized by different colours of their hypocotyls, ranging from white to black, that are involved in different biological properties (Gonzales et al. 2005, 2006a; Rubio et al. 2006). Most of experimental data in literature reports the effects mainly of the red, yellow and black hypocotyl types (Gonzales et al. 2006b, 2007, 2009). Bibliographic data show studies in which the three primary phenotypes of Maca (Yellow, Red and Black) determine different biological effects.

The edible part of the plant is the hypocotyl, like tuber, that can be used both fresh and dried, the Peruvian native population eats dried Maca. Fresh hypocotyls are boiled in water to obtain a juice or they are subjected to naturally and traditional open-field drying. Maca hypocotyls are exposed at strong light conditions, at atmospheric pressure typical of the high altitude, and at extreme temperature for two months. After drying, hypocotyls are washed, ground and a flour with a particle size of 0.8 mm is obtained and stored until use (Tafuri et al. 2019).

Biological properties of Maca gathered from experimental and clinical studies on this species, reveal the importance of this plant as nutraceutical food (Valerio and Gonzales 2005; Ciani et al. 2018). In the dried hypocotyls of Maca, high valuable nutritional elements, as carbohydrates, proteins, lipids, essential amino acids and free fatty acids, known as primary metabolites, are present (Gonzales 2012; Tang et al. 2019). Furthermore, Zheng et al. (2000) reported several secondary metabolites such as macaridine, macamides, Maca alkaloids and glucosinolates, typical of this plant. The secondary metabolites are responsible for the biological and medicinal properties of the Maca (Gonzales 2012; Tafuri et al. 2019). Several aromatic glucosinolates are found in the Maca such as benzyl glucosinolates (glucotropaeolin) and *m*-methoxybenzyl glucosinolate (glucolimnathin). Therefore, the several biological effects of Maca depend on the kind of the hypocotyl and the different secondary metabolite concentrations, hence the phytocomplex (Gonzales et al. 2005, 2012; Clément et al. 2010a; Ye et al. 2019).

Many studies report positive effects of Maca on the sexual activity of man and woman, such as libido and sexual performance (Gonzales et al. 2007, 2012). Also, the aphrodisiac action of Maca has been demonstrated, in rats and mice with erectile dysfunction. An oral dose of purified Maca lipid extract for 22 days resulted in an improvement of erectile function in all treated animals (Zheng et al. 2000). This result was probably attributed to the action of alkamides, macamides 1, 2, 3 and 4, isolated and identified in the root as reported by Clément et al. (2010a, 2010b). Maca also modulates the symptoms of menopause in independent manner on estrogen and testosterone production (Brooks et al. 2008).

Gonzales et al. (2005) showed that administering aqueous extract of Red Maca reduced ventral prostate size in normal and testosterone enanthate treated rats. Furthermore, a study on adult male rats exposed for 21 days at an altitude of 4340 m above sea level and treated with an aqueous extract of Maca, showed an increase in the number of spermatozoa and also a prevention high altitude-induced

spermatogenic disruption (Gonzales et al. 2004). Furthermore, Black and Yellow Maca studies report an involvement in spermatogenesis, memory and fatigue, with increased memory and learning in mice (Rubio et al. 2007). Our research group has shown that dietary supplementation with Yellow Maca powder improves semen production in the horse. Also, the semen taken from stallions treated with Maca was more resistant to cooling and storage (Cocchia et al. 2010; Del Prete et al. 2018a). The presence of particular secondary metabolites is responsible for the Maca action on the production and improvement of sperm quality (Clément et al. 2010a, 2012). The presence of glucosinolates and macamides, allows the Maca to protect cells from oxidative stress. Reactive oxygen species (ROS) are produced in mammalian body (Ciani et al. 2015; Tafuri et al. 2018); in the testes are produced in normal spermatogenesis and steroidogenesis. The physiological production of ROS is involved in the capacitation, hyperactivation, acrosome reaction and sperm-oocyte fusion to allow effective fertilization, whereas high levels cause ATP depletion, loss of sperm motility and viability (Tafuri et al. 2015). The antioxidants block the harmful effects arising from ROS, but if the production of these is massive oxidative stress occurs (Costantino et al. 2009; Cocchia et al. 2015; Del Prete et al. 2018b). Recently, Zhang et al. (2019) showed that the combined extracts of *Lepidium meyenii* and *Allium tuberosum* Rottl. had a synergic effect improving erectile dysfunction in male mice.

Despite the exact mechanism of action of Maca is still unknown, the research conducted so far clearly indicates that the bioactive compounds of Maca produce the previously described effects and a whole state of wellness.

The aims of this review are to summarize and elucidate the current state of knowledge on the biological properties and the evidences from experimental and clinical studies of *Lepidium meyenii* (Maca) on male reproduction.

2. Maca and male reproduction

Maca is widely known for both its nutritional and fertility-enhancing properties and, traditionally, it is consumed after a natural drying process. Esparza et al. (2015) showed that the traditional drying process was necessary to allow the formation of bioactive metabolites which are absent in the fresh Maca.

In experimental studies, aqueous extract of Maca resulted only effective after boiling pulverized Maca hypocotyls in water. Furthermore, in a dose-response study in rats, it was reported that Maca extract administered in doses up to 5 g/kg was safe and that in addition a greater effect on the reproductive parameter was obtained by administering a dose of 1 g of extract/kg corresponding to 2.2 g of dried Maca hypocotyls/kg (Chung et al. 2005).

As known, Maca presents different ecotypes in relation to the different colour of its hypocotyls. Furthermore, different biological properties have been attributed to different colours. In particular it has been reported that both Black Maca and Yellow Maca determine beneficial effects on spermatogenesis in rats (Gonzales et al. 2006b), while, Red Maca reduces the size of the ventral prostate and prevents prostatic hyperplasia in rats (Gonzales et al. 2007; Gasco et al. 2007).

2.1. Effects on spermatogenesis

Many studies have reported that Maca may increase daily sperm production, epididymal sperm count or vas deferens sperm count in healthy rats (Gonzales et al. 2001a) and in rats with experimental-induced spermatogenesis disorders (Gonzales et al. 2004; Bustos-Obregon et al. 2005; Rubio et al. 2006).

Gonzales et al. (2001a, 2003a) observed, in male rats, that oral administration of an aqueous extract and ethanolic extract of Maca for 21 days improved spermatogenesis in spermatogonial mitosis acting on its initial stages (IX-XIV) and increasing weight of testis and epididymis. The same effects in normal man treated for 4 months without affecting serum testosterone and oestradiol levels were observed (Gonzales et al. 2001b).

Gonzales et al. (2006a) showed that Black Maca was the only phenotype that increased daily sperm production and epididymal sperm motility after 42 days of treatment. Results from another study performed on rats (Gonzales et al. 2006b) showed that, during a spermatogenic cycle (12 days), aqueous extract of Black Maca improved sperm count in epididymis as early as 1 day after treatment and that this effect seems to be a regulatory mechanism of the distribution of sperm produced in the testis rather than a real higher production of sperm. Gasco et al. (2007) performed a study on the three varieties of Maca to evaluate the chronic effects (84 days of treatment) on daily sperm production, sperm count in epididymal and vas deferens and total DNA levels in testes of male rats. The results confirmed that Yellow and Black Maca improved epididymal sperm count and all the three ecotypes increased sperm count in vas deferens without affecting daily sperm production. The testis DNA levels were not affected by treatment of any of three varieties.

Gonzales et al. (2013a) have reported that Black Maca increased epididymal sperm count as early as 3 days after treatment. Precisely, the increment of spermiation stages (VII-VIII), germinal cell mitosis (IX-XI), daily sperm production and epididymal sperm count were observed, without affecting the levels of testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH).

The greatest effect on spermatogenesis was observed with ethyl acetate fraction of Black Maca hydroalcoholic extract (Yucra et al. 2008). The effects of Yellow Maca aqueous extract on animals with experimental damage of spermatogenesis demonstrated that Maca prevented high altitude-induced spermatogenic disruption in rats exposed to high altitude (Gonzales et al. 2004), lead acetate-induced spermatogenic disruption and the deleterious effect of administration of Malathion on spermatogenesis in mice (Bustos-Obregon et al. 2005; Rubio et al. 2006) and improved motility and sperm count in mice with induced subfertility after administration of ketoconazole (Valdivia-Cuya et al. 2016).

An interesting research by Sanchez-Salazar and Gonzales (2018) analysed the sperm count in mice treated with boiled aqueous extract of Yellow Maca hypocotyls from different sizes, under different pH conditions and using two different routes of administration (oral and intraperitoneal). The data showed that sperm count was higher in mice receiving Maca from the larger sizes and that reduction in Maca extract pH increased sperm count. Moreover, the study suggested that an oral administration of the aqueous extract of the hypocotyls was more effective because its passage in the

gastrointestinal tract allows the conversion of the compounds present in Maca into bioactive principles with therapeutic action.

In the bulls, food supplementation with Maca for 20 weeks had no direct effect on body weight, testes circumference, rectal temperature, mating behaviour and ejaculate volume; however, improved sperm quantity, quality and DNA fragmentation index (Clément et al. 2010b).

A recent study, conducted by our research group, showed for the first time that diet supplementation with Yellow Maca powder, given to 5 stallions for 60 days, improves semen production. Furthermore, the semen from Maca-treated stallions was more resistant to cooling and storage, preserving acrosome and DNA integrity and total and progressive sperm motility (Del Prete et al. 2015, 2018a; Ciani et al. 2017).

2.2. Prostate function

Red Maca has proven to reduce prostate size in rats and mice with testosterone enanthate induced hyperplasia (Gonzales et al. 2005, 2008). Gonzales et al. (2005) reported that after 42 days of treatment with Red Maca, the ventral prostate weight was reduced more than 50% and the increased seminal vesicles weights induced by testosterone enanthate was not affected. It was also noted that Red Maca affected ventral prostate size without modifying serum testosterone or oestradiol levels, this suggested that the Maca interfering the androgen action beyond the receptor. Moreover, it was observed that Red Maca reversed the action of testosterone enanthate more efficiently than the convention treatment (Gasco et al. 2007).

Another study demonstrated that the *n*-butanol and aqueous fractions of Red Maca methanolic extract had different effects in rats with testosterone induced benign prostatic hyperplasia (Fano et al. 2017). *N*-butanol fraction, but not aqueous fraction or methanolic extract, reduced prostate size in benign prostatic hyperplasia by restoring expression of ERβ without affecting androgen receptors and ERα.

The effect of Red Maca on benign prostatic hyperplasia seems related to the content of benzyl glucosinolate. Both Red Maca aqueous extract and hydroalcoholic showed some similarities in effects, in fact, both extracts of Maca reduced the prostate weight in rats with prostatic hyperplasia induced by testosterone enanthate (Gonzales et al. 2007).

2.3. Sexual behaviour

In 2000, Zheng et al., revealed for the first time an aphrodisiac activity of Maca (Zheng et al. 2000). Lipidic extract of Maca, administrated for 22 days, increased the number of complete intromissions and the number of sperm-positive females in normal mice, and decreased latent period of erection in male rats with erectile dysfunction. Cicero et al. (2001) found that pulverised Maca hypocotyls oral administration in different doses (15,25,75 and 100 mg/kg) for 21 days on rats increased sexual behaviour, during both acute and chronic treatments, independently from its action on spontaneous locomotor activity. On the contrary, Lentz et al. (2007) detected no significantly changes in male sexual behaviour during acute and short-term treatments and did not

found any effects during long- term treatment from the first to the last day of treatment with Maca powder.

Hexanic extract of Maca administered sub acutely improved effectively sexual behaviour in sexually inexperienced rats (Cicero et al. 2002). Aphrodisiac action has been demonstrated in rats and mice with erectile dysfunction that were treated with an oral dose of purified Maca lipid extract for 22 days. After treatment, an improvement in erectile function has occurred in all treated animals. This result was attributed to the action of four alkaloids, macaine 1, 2, 3 and 4, isolated and identified in the root (Clément et al. 2012).

Lavana et al. (2013) studied for the first time the effect of Maca supplementation on some libido and semen characteristics of hair sheep rams (*Ovis aries*). The experiment showed the increment of some mating behaviour while semen appeared unaffected.

A double-blind placebo-controlled, randomised, parallel clinical trial, in which active treatment with different doses of gelatinized Maca compared with placebo, was conducted on men for 12 weeks. The research revealed an improvement of sexual desire at 8 and 12 weeks of treatment, independently of changes in Hamilton scores for depression or anxiety and not affecting serum testosterone and oestradiol levels (Gonzales et al. 2002, 2003b); Maca also improved mood, anxiety and increased activity (Gonzales 2006c). A second double blind, randomised clinical performed on men with mild erectile dysfunction, treated with Maca for 12 weeks, showed an improvement on the subjective perception of general and sexual well-being (Zenico et al. 2009).

Gonzales-Arimborgo et al. (2016) have demonstrated that consumption of a spray-dried extract of Red and Black Maca for 12 weeks resulted in an improvement of mood, energy, and health status in humans. Effects on mood, and energy were better with the spray-dried extract of Red Maca.

3. Discussion

In the contemporary society, male sexual dysfunction is a serious public health problem which affects negatively relationships and the psychological health. Especially erectile dysfunction is increasing in man of all ages and is correlated, among other causes, to an unhealthy lifestyle (Abdulsalam et al. 2019). Many types of drugs are commonly used in order to improve sexual function; however, their well-known negative side effects increased the interest in alternative therapies.

Maca has been used for centuries, from the Andean population, as a food supplement for its incredible nutritive and medical properties. In recent decades, the interest in Maca has increased and has made it a nutraceutical of great fame for its benefits on health and, for this reason, Maca is exported worldwide as powder, capsules, pills, flour, liquor and extracts.

Maca showed effects on sexual behaviour, fertility, mood, memory, osteoporosis metabolism and treatment of some cardiovascular diseases and tumour. Several researches suggest that different phenotypes (Red, Black and Yellow Maca) are associated with different biological effects and medical targets (Table S1). For example, the Red Maca variety reverses benign prostatic hyperplasia in mice and experimentally

induced osteoporosis (Gonzales et al. 2014) and show usefulness in stimulating sperm count (Gonzales et al. 2006b). Black and Yellow Maca show the best results on spermatogenesis, memory, and fatigue, with increases in memory and learning in mice (Rubio et al. 2007). Additionally, Black Maca reduces glucose levels, and consumption of this variety is associated with lower blood pressure and an improved health score (Gonzales et al. 2013b). The effects of Maca depended on many factors including different phenotypes, cultivation region, harvest time, product process and the variety and the proportion of its bioactive compounds.

4. Conclusion

Lepidium meyenii, an edible root plant that grows in the Andean region of Peru, has been used as a dietary supplement for its nutritional and therapeutic properties. In the present review a variety of research, which investigated the effects of Maca on male reproductive tract, was reported. In recent decades, the interest in Maca has increased and has made it a nutraceutical of great fame for its benefits on health and, for this reason, Maca is exported worldwide as powder, capsules, pills, flour, liquor and extracts.

Despite the numerous studies conducted on animals and human, further research is required to elucidate the mechanisms of action of Maca phytocomplex and of each bioactive component alone or in association.

Disclosure statement

No potential conflict of interest was reported by the authors.

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