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Lepidium meyenii (Maca) – multidirectional health effects – review

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ABSTRACT

Lepidium meyenii, commonly known as Maca, is a Peruvian plant that grows high in the Andes, in areas over 4,000 meters above sea level. Its composition contains almost all of the essential amino acids and twenty of the essential fatty acids needed by man, as well as many vitamins, minerals and several sterols and glucosinolates. The specific and unique unsaturated acids and amides found only in this plant are the macaenes and macamides. Most valuable ingredients are contained within the hypocotyls. Maca comes in three forms, based on its root colour, yellow, red and black. Although used individually, consumption recommendations are usually for a mix of all three. Since Inca times, it has been considered as super food.

Although now mostly used in the form of a supplement, ongoing research does not exclude future applications of Maca as medicine. It is attributed to have an effect on male fertility (adding energy and vitality), and in regulating hormone secretion. In animal studies, Maca has been shown to have antioxidant, neuroprotective effects and antiviral activity. Moreover, it has been demonstrated to alleviate the effects of depression. In addition, there are reports that Maca reduces the development of cancer and osteoporosis, improves memory, facilitates concentration and alleviates the symptoms of menopause. The obtained results, however, require further analysis to confirm its effect. Currently, there is little information on toxicity, so there is a need for specialized research in this area, and on-going research concerns the most effective variety and form of preparation of Maca for administration to achieve best effects. The potential of Maca as medicine exists. The increasing pan-continental popularity of Maca has created the need for a better understanding of its action mechanisms.

INTRODUCTION

Maca, known in science as *Lepidium meyenii* Walpers, is a Peruvian plant growing naturally in areas above 4,000 meters in the Peruvian Central Andes. It belongs to the Brassicaceae family. The name *Lepidium meyenii* Walpers has been used since 1843, when German botanist Gerhard Walpers deposited the first holotype of this plant [1].

Maca contains many proteins, amino acids, fats and vitamins [2], as well as a variety of secondary metabolites such as maca ene, alkaloids (including maca amide), glucosinolates, and other components [3-5]. It is also a rich source of micro- and macroelements, including iron, calcium,

copper, zinc and potassium. Maca has been used by local people as a food ingredient and in traditional folk medicine to enhance sexual function, fertility, energy, alertness, mental concentration, mood and physical immunity [6,7]. Maca is now marketed in Asia, Europe and North America.

Maca studies have been mostly conducted on animal models, although a few human trials exist in the literature. Due to its multifaceted effect as a natural remedy, it is receiving more attention and thus has become the subject of much research. Some review was carried out by GF Gonzales *et al.* [7], however, we have consolidated the latest reports in the context of the growing demand for Maca. This article, therefore, discusses the impact of Maca on humans, animals and selected cell lines. Our research has been carried

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out since 2007, and our listing includes the type of Maca, the particular plant part source and the type of extract. In our work, we list the studies in which Maca has been tested for its specific use as a sunscreen, for fertility needs, for treatment of erectile dysfunction, for enhancement of memory and for anti-viral activity. In such works, its antioxidant properties were also evaluated. A comparison of selected studies is shown in Table 1.

ULTRAVIOLET RADIATION PROTECTION

The protective effect of yellow Maca to ultraviolet radiation (UVR) was tested on 3-month-old male Holtzman rats. Herein, a topical boiled water extract had the strongest effect. In control animals, exposure to UVR rays resulted in the thickening of the epidermis. In experimental animals, epithelial height after dermal application of aqueous extract, were significantly lower in comparison with the control group. There were no differences in skin thickness between that of animals treated with aqueous extract and non-irradiated control. The effect was independent of the type of radiation [8]. The dose response was observed in the case of UVA, UVB and UVC radiation, with a better effect than that observed with commercial sunscreen. As the authors of the experiment suggest, the protective substances for the types of radiation used are the polyphenols and glucosinolates present in the Maca's aqueous extract. The authors also suggest that Maca is an effective agent for ameliorating UVC-mediated damage. Further research is, however, needed about the UV protection mechanism, but enough information exists to suggest its commercial application in sunscreens.

EFFECT ON SPERMATOGENESIS

The effects of aqueous Maca extracts on spermatogenesis have been the subject of research. Three types of Maca were tested: black, yellow and red. The study was conducted on 4-month-old male Holtzman rats. In the work, administration of boiled water extracts of yellow and red Maca as a gavage did not produce any effect, while a black Maca gavage seemed to have a beneficial effect on sperm counts and their motility [9]. Experimental results showed that after 42 days, sperm production was significantly higher, and while sperm motility was unchanged after 7 days of treatment with either of the three types of Maca [10,11], after 42 days of treatment with black Maca extract, the sperm motility was higher than in that of other groups. Testosterone and estradiol hormonal levels remained unchanged during the study.

Research by Ohta *et al.* provides additional information. Herein, young male Wistar rats of the experimental group were given in diet, a powdered Maca water-alcohol extract (a combination of yellow, black and red Maca, with the commercial name, MACAXS™) for 6 weeks. This study demonstrated that administration of a water-alcohol extract of Maca for 42 days elevated serum testosterone levels, although reports from other have not always confirmed this. The weight of the seminal vesicle also increased, but this could be due to enhanced testosterone levels as the seminal vesicle is sensitive to testosterone. The prostate gland remained unchanged, but serum testosterone concentration were elevated, suggesting that Maca can stimulate Leydig cells especially in the metabolic process of cholesterol [12,13]. Moreover, the weight of the rats increased progressively regardless of the diet used, suggesting that Maca does not affect b.w., although animal observations have also shown

Table 1. Comparison of selected studies

Type of Maca	Plant Part	Origin	Type of extract	Study subjects	Results	References
Yellow	Dried hypocotyls	Pasco, Peru	mixed in water	Rats	Dermal protection against UV radiation was shown; the most effective - boiled maca	[8]
			water boiled extract			
Yellow, Red	Dried hypocotyls	Carhuamayo, Junin, Peru	water boiled extract	Rats	No effect	[9]
Black					Increase in sperm mobility	
Black	Dried hypocotyls	Carhuamayo, Junin, Peru	hydro-alcoholic extract	Mice	Inhibition of memory disorder	[16]
No data	Powdered root	Pampas Valley (Tayacaja, Huancavelica)	methanol extract	Cell lines	Inhibition of influenza viruses a and b	[22]
Black	Dried hypocotyls	Carhuamayo, Junin, Peru	water boiled extract, frozen and lyophilized	Mice	Improved learning and memory in mice	[17]
Black, Yellow, Violet	Dried plant	Juhua Village market Kunming province, Yunnan	petroleum ether extract	Rats	Strong antioxidant effects (purple Maca) in rats	[23]
Red, Yellow, Black	Dried hypocotyls	Carhuamayo, Junin, Peru	water-boiled extract	Rats	Increases in sperm cell count, increases in body weight in animal models	[10]
No data	Dried root	Kunming, China	polysaccharide mp21	Cell lines	Immuno-stimulating effects, increased macrophage activity	[26]
No data	Dried hypocotyls	Arequipa, Peru	methanol extract	Cell lines	Neuroprotective effects	[18,20]
	Leaves	Ramancancha, province of Junin, in the Junin Department		Rats		
No data	No data	Peru	no data	Mice	Regulation of autophagy proteins, slow down of cognitive decline associated with age	[19]
Yellow	No data	Ecoandino SAC Co. Lima, Peru	lipid extract	Rats	Improvement of physical condition by suppression of oxidative stress	[25]
No data	No data	Quimica Suiza, Peru	powder	Rats	Reduction of plasma cholesterol, VLDL, LDL and TAG	[24]
No data	Root	Junin, Peru	powder	Womans	Suppression of menopausal symptoms	[15]
No data	Root	Lima, Peru	powder	Men	No effect on the level of sex hormones	[11]
No data	No data	Linzi, Xizang, China	petroleum ether extract	Mice	Antioxidant effect in brain tissue	[29]
Black, Red, Yellow	Dried bulb	MACAXS™ (TOWA Corporation K.K., Tokyo, Japan)	hydro-alcoholic powder extract	Rats	Stimulation of male sex hormones	[12]

that Maca can stimulate appetite on a continuous basis. More recent studies, however, suggest that long-term administration of MACAXS™ induces only a temporary increase in serum testosterone in adult male rats [14].

Gasco *et al.* conducted an animal study using yellow, red and black Maca to evaluate the effects of these substances on daily sperm production and total sperm DNA concentrations. In the study, 3-month-old male Holtzman rats were used, as were water extracts of Maca. The results indicate that after 84 days of treatment, Maca modulates the number of spermatozooids at the level of reproductive tract, while in the epididymis and deferent duct, the number of sperm cell increases. No changes were observed in daily sperm production. These studies suggest that Maca may prevent sperm reduction in the epididymis as observed in animals without copulatory activity. The weight of the genitals did not change, and no apoptotic changes in cells of the spermatogenesis series or DNA modification at the nucleus level [10] was reported.

In another randomized double-blind placebo-controlled study of 12 weeks, men aged 21 to 56 were involved. They were given Maca for 2, 4, 8 and 12 weeks. The results indicate that Maca did not modify testosterone levels, luteinizing hormone, follicle stimulating hormone, prolactin, 17-alpha hydroxyprogesterone and 17 beta-estradiol. The results suggest that Maca did not affect serum sex hormone levels in men [11].

EFFECT ON MENOPAUSAL SYMPTOMS

Some researchers have investigated the use of Maca in the relief of the symptoms of menopausal discomfort that women experience in early menopause. H.O. Meissner *et al.* have prepared Maca capsules through pre-gelatinization of a starch component so as to generate a product of appropriate density for facilitating digestion. In their testing, a set of double-blind, placebo-controlled clinical trials were performed with twenty Caucasian women in early menopause (a three month trial) and eight volunteers aged 45-62 years (a nine month trial). In this study, several serum hormone profiles were analyzed, including luteinizing hormone (LH), follicle stimulating hormone (FSH), estrogen (E2) and progesterone (PG). The Green Menopause Index was also administered. This is a list of questions that in women is used to assess menopausal symptoms such as hot flushes, night sweats, fast heart rate and difficulty falling asleep.

The results showed a reduction in menopausal symptoms, and most women observed a noticeable reduction in the discomfort typical of menopause, as well as reduced nervousness, less difficulty in falling asleep, better concentration, improved ability to concentrate, a feeling of being more energetic, less frequent numbness and headaches, and reduced night sweating, as well as a lower level of TSH (*thyroid-stimulating hormone*) when the product was administered in the short and long term. The increase in progesterone was insignificant, but significant increase was seen in blood LH and Eg levels [15]. The authors suggest that in the future, Maca administration in such a capsule form may be an alternative to hormone replacement therapy (HRT).

MEMORY

One study examined the effect of aqueous Maca black extract on memory impairment as induced in ovariectomized mice. Therein, cognitive functions and neuroprotective effects were also analyzed. The study was conducted on 3-month-old female mice. The animals were administered the extract orally for 35 days. This resulted in an increase in latency time and a decreased in the number of committed errors as demonstrated in the step-down avoidance test. Administration of the Maca extract improved results in the Morris water maze as well [16]. Studies indicate that Maca contains polyphenol as an antioxidant. This has been shown to reduce the oxidative stress caused by reactive oxygen species that brain tissue is sensitive to. As a result, the authors suggest that administration of aqueous Maca extract has a positive effect on learning.

In another study, the effect of a water-alcohol extract of black Maca was assessed on improving scopolamine-induced memory impairment in 3-month-old male mice. Memory status was analyzed using the Morris water labyrinth and the step-down avoidance test. Herein, mice which had consumed a black Maca aqueous or hydroalcoholic extract showed a shorter overall swimming distance and better delay avoidance as compared to scopolamine-treated mice controls [16]. However, Maca did not alter MAO (*monoamine oxidase*) activity in any of the applied doses in the test mice, but AChE (enzyme acetylcholinesterase) activity was reduced by more than 45%. The results of this study suggest that Maca helps in learning and memory. No side effects were reported.

In subsequent studies, the effect of response was assessed to the dose of black Maca water-alcohol extract in mice treated with 20% ethanol (EtOH) as a memory loss model. Herein, the extract was administered orally to 3-month-old male mice for 28 days. The open field tests and the Morris water labyrinth showed Maca's inhibitory effect on ethanol as a memory impairment. In both tests, in the animals receiving black Maca extract, a shorter time was observed during escape attempts and in evacuation [17]. The findings suggest that the greater the dose of Maca, the better the temporal effect of these behaviours.

Other researchers, while experimenting on 14-month-old male mice, also suggest that supplementation with Maca increases cognitive function [18]. In this study, the animals were given powder Maca by probe over a period of 5 weeks. After this period, the level of individual proteins in the tissues of the examined animals was analyzed. The results showed that Maca supplementation induced the growth of individual subunit proteins of nervous tissue. Enhanced levels of LC3-II (light chain) protein, as well as an increase in LC3-II/LC3-I ratio, and an elevation in the levels of ATG 7 (autophagy-related protein 7) were reported. It is thought that Maca induces an upregulation of autophagic proteins in the cortex, hence enabling programmed cell death. The authors also suggest that the neuroprotective effect of Maca comes about by improving mitochondrial respiration [19].

NEUROPROTECTIVE EFFECTS

Maca pentane extract mainly contains lipo-soluble alkaloids, benzyl amides (macamides), polyunsaturated fatty acids (macaenes) and benzylisothiocyanates. These, when administered intravenously, can reach the brain in a higher concentration than through other routes of intake. In one study, rats administered doses of Maca at 10 and 30 mg/kg b.w. showed significantly less tumor induced neuronal damage [18]. Moreover, the authors demonstrated that the pentane Maca extract was responsible for normal dendritic cell shapes. In addition, the researchers found that Maca reduces the risk of heart attack. In the study, a dose of 30 mg/kg b.w. also had a neuroprotective effect.

In such studies, most of the antioxidant activity of a Maca Methanolic extract was observed in the aqueous fraction. Maca has been found to exhibit a neurobiological effect in vitro, increasing cell viability and reducing cytotoxicity against oxidative stress generated by 6-OHDA (*6-hydroxydopamine*) [20]. Several studies suggest that Maca strengthens the mechanism of oxidation and reduction enzyme balance by increasing the enzyme activity of superoxide dismutase and by direct free radical scavenging, such as that of nitric oxide.

In one study, the neuroprotective ability of Maca methanol extract in a Parkinson's cell model was evaluated. Herein, the experimenters induced neurotoxic damage in PC12 cells using dopamine analogue (DA) and 6 OHDA. In cell viability assays, pretreatment with Maca extract increased cell viability, especially at a dose of 10 µg administered over 12 hours (85.1%, $p < 0.001$) [20]. The authors suggest that Maca can suppress Parkinson's disease by slowing down cognitive decline associated with age, probably through a mitochondrial-mediated mechanism, and by increasing autophagy-related proteins [19]. The authors also observed an increase in SOD activity in cells pre-treated with Maca extract, suggesting that Maca's neuroprotective effect may be associated as well with inhibition of oxidative stress by inhibiting free radical activity [21].

ANTIVIRAL ACTIVITY

Maca antiviral activity was studied via MDCK (Madin-Darby canine kidney) cell lines, and the tests were performed on human influenza A and B viruses. The results were satisfactory and promising. Maca extract showed no MDCK cell toxicity, and Maca concentration at 10-80 µg/ml was effective in antiviral activity by restoring the normal growth of MDCK cells [22]. It is thought that the antiviral component of maca either interferes with the attachment of the virus to the cells or it prevents the virus from fusing with the cell. In the work, evaluation of protein levels on the infected cell surface was a point direction for infection control. Maca was also found to decrease viremia levels.

ANTIOXIDANT EFFECT

In a study, petroleum ether extracts of Black, yellow and purple Maca were administered at 100 mg/kg for 90 days to diabetic Wistar rats. Herein, previously identified in

the extract analogies were macamides, the highest content of which was in the extract of black Maca. After 60-days, TBARS (thiobarbituric acid reactive substances) and carbonylated (CP) proteins were reduced, hence, lipid oxidation was also diminished in the diabetic rats [23]. Maca extracts also increased the activity of SOD (superoxide dismutase) and CAT (catalase) antioxidants, and enhanced the number of erythrocytes in the tested animals. Of all the types studied, the extract of purple Maca showed the strongest antioxidant activity in this experimental model.

In another study, Wistar rats underwent oral administration with a 1% Maca solution along with a high-sugar diet. The authors used rats with plasma glucose levels above 14.82 mmol/L. During the supplementation, very low-density lipoprotein (LDL), total cholesterol, serum triacylglycerol (TAG) levels, as well as VLDL (Very Low Density Lipoprotein) levels in the liver were observed. In addition, supplementation with Maca resulted in a decrease in blood glucose levels. The authors suggest that Maca may be used in the treatment and prophylaxis of chronic conditions characterized by atherogenic lipoprotein profiles, hepatic steatosis, antioxidant disorders and conditions with impaired glucose [23,24].

In yet one more study, soluble yellow Maca lipid extract containing macamides was evaluated. Herein, the studies were performed in rats treated at 100 mg/kg b.w. and the influence of lipid extract on swimming and energy depletion in animals was assessed. As a result, reduced serum LDH (lactate dehydrogenase) levels, muscle damage index, and TBARS were observed in lipid-induced muscle tissue lipid oxidation. However, the level of catalase in the liver and (glutathione) GSH antioxidant in muscle and liver were higher than in the control group that was not treated with Maca [25]. The study conclusion was that feeding the Maca extract for a period of 3 weeks significantly improved swim strength and endurance in a dose-dependent manner. The authors suggest that this effect depends on the effect of Maca extracts on suppression of post-exercise oxidative stress [25].

IMMUNOMODULATION

In a study using the DEAE-52 column and Sephacryl-500 TMS, Maca polysaccharides (MP21) were extracted. These consist essentially of rhamnose, arabinose and galactose. In vitro studies have shown that MP21 showed indirect HEPG-2 (human liver cancer cell line) cytotoxicity by stimulating macrophage responses. Extracted MP21 had strong immunomodulating properties and strongly activated macrophage activity [26]. In addition, MP21 polysaccharides mediate the production of various effector molecules that may contribute to their antitumor activity [26]. Furthermore, MPS-1 and MPS-2 polysaccharides in MM counteract fatigue, but the mechanism of action has not yet been recognized [27]. In addition, according to the latest reports, the MC-2 polysaccharide that was isolated from Maca can be an effective tool in the fight against cancer. Further studies, however, are necessary to assess the effect of other individual compounds contained within Maca [28].

ANTIDEPRESSANT EFFECT

A study conducted on 90 male 60-day-old Kunming mice showed that Maca has a clear influence on the behavior of mice exposed to chronic stress. In the work, Maca extract was administered orally at doses of 125, 250 and 500 mg/kg b.w., while fluoxetine (10 mg/kg b.w.) was used as a positive control. After treatment with Maca, especially at higher doses, a significant reduction in corticosterone levels in the serum of mice was observed. In the studied brain tissue of animals taken after 6 weeks, increased levels of nor-adrenaline and dopamine were seen. In contrast, the activity of reactive oxygen species was significantly reduced. The authors point out that Maca may be used in patients with depression, although further research is needed to identify specific compounds that cause such effects [29].

SUMMARY

Maca is a plant with high potency as an adaptogen and appears promising as a natural remedy in the prevention of many diseases [30]. Dried Maca is rich in amino acids, mineral salts, iodine, iron and magnesium, and Maca owes its properties to this unique composition of ingredients. Maca contains many effective antioxidants and can be used as a functional food [31]. Moreover, recent studies suggest that the main polysaccharide in Maca, MP-1, possesses the potential to be a food or drug to prevent alcoholic liver damage (ALD) in humans [28].

Maca is also surprisingly effective in improving memory and learning. Even more promising are studies showing its neuro-protection effects. However, in recent reports, it seems that Maca's effect on reproductive capacity has been exaggerated. Still, there is a lack of sufficient research on humans in order to provide an unambiguous answer [32].

The research that has been carried out has shown that Maca has tremendous potential, but more research is needed in various fields of study, including biomedical research, prior to its recommendation. Some of these studies need to be done at the molecular level. What is more, while Maca has not been shown to be harmful or toxic, further research is also needed in this direction.

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