Maca: An Andean crop with multi-pharmacological functions

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Abstract

Maca (Lepidium meyenii walp.), a biennial herbaceous plant of the family Brassicae, which is cultivated mainly in the central Andes of Peru, has been used as both a food and a traditional medicine in the region for over 2000 years. The subterranean parts of the plant have long been used as a staple foodstuff by indigenous peoples in the Andean region, but the plant is also valued for its medicinal role. As is usual with many traditional “folk” medicines, many claims have been made regarding the efficacy of maca in treating a wide range of illnesses and medical conditions. However, in the 20th century most scientific attention has been focused in the areas where the pharmacological actions of maca seem most strongly attested, these include, enhancement of sexual drive in humans, increasing overall vigour and energy levels, and increasing sexual fertility in humans and domestic livestock. Since the early days of the 20th century numerous scientific studies have been carried out into the basis of its pharmacological action in these areas. In this review, the composition and pharmacological function of maca are systematically discussed. Additionally, the current discussion surrounding its mode of action in the areas listed above is also presented.

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Keywords: Composition; Maca (Lepidium meyenii walp.); Pharmacological functions; Secondary metabolites; Toxicity

Contents

1. Introduction ........................................................................................................................................... 00
2. The composition of maca ..................................................................................................................... 00
   2.1. Macaene and macamide ................................................................................................................. 00
   2.2. Glucosinolates and their derivatives ............................................................................................... 00
   2.3. Alkaloids ....................................................................................................................................... 00
   2.4. Sterols .......................................................................................................................................... 00
   2.5. Other compounds .......................................................................................................................... 00
3. The biological activities of maca ........................................................................................................ 00
   3.1. Improving fertility ......................................................................................................................... 00
   3.2. Improving sexual performance ..................................................................................................... 00
   3.3. Anti-proliferative function ............................................................................................................ 00
   3.4. Role in vitality and stress tolerance ............................................................................................... 00
   3.5. Improving growth rate .................................................................................................................. 00
   3.6. Anti-postmenopausal osteoporosis ............................................................................................... 00

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1. Introduction

Maca (Lepidium meyenii walp.), belonging to the family of Brassicaceae, is an annual or biennial herbaceous plant. It is mainly domesticated in the central Andes of Peru at elevations of 3500–4500 m above sea level, a zone characterized by areas of barren, rocky terrain, intense sunlight, fierce winds, and freezing temperatures. In this inaccessible and intensely cold habitat, few other crops survive with the exception of some highland grasses, and a few hardy members of the Solanaceae (Flores, Walker, Guimaraes, Bisd, & Vivanco, 2003). Domesticated maca has been grown in Peru for at least 2000 years ago, but little is known about its origin. There are eight or more different ecotypes in the cultivation area, distinguished according to the color of their roots, such as, yellow, purple, white, grey, black, yellow/purple and white/purple (Gonzales et al., 2006; Rea, 1994). The yellow ecotype is the commonest cultivar in this region.

The subterranean part (hypocotyls) of maca is edible, and is a staple food for the indigenous peoples of this arid zone. Maca 'hypocotyls' are eaten fresh, or can be dried and stored for later consumption. The dried roots can be eaten after boiling in water or milk, or made into juices, cocktails, alcoholic beverages or maca coffee (Ochoa & Urgent, 2001; Quirós & Cárdenas, 1992; Rea, 1994). However, maca is not only used as a foodstuff, but it is also used as a traditional medicine, especially as an aphrodisiac to enhance sexual drive and female fertility in human beings and domesticated animals. During the conquest of the Inca Empire, the Spaniards fed their horses with maca to help minimize the reduction in reproductive ability at high altitudes. Inca warriors were said to be fed with maca to increase their energy and vitality, they were prohibited from consuming after the conquest of a city it as a measure to protect women from their sexual impulses (Quirós & Cárdenas, 1992). Maca also has other claimed medicinal properties, according to traditional beliefs, such the capacity to cure or relieve rheumatism, ameliorate respiratory ailments, may act as a laxative, is said to regulate hormonal secretion, stimulate metabolism, lead to memory improvement, possess antidepressant activity, and effectiveness in combating anemia, leukemia, AIDS, cancer and alcoholism among others (Quirós & Cárdenas, 1992). This extensive list of claims is characteristic of many folk medicines, but given the current drive for effective new drugs from natural sources, clearly indicates the reason behind the many scientific studies into maca's composition, and its potential pharmacological actions.

2. The composition of maca

The composition of maca has been analyzed and elucidated using HPLC/UV, HPLC/MS, GC/MS, ESI/MS, ESI/HRMS, NMR and so on. Maca is abundant in protein, unsaturated fatty acid and minerals. Fresh maca roots have more than 80% water content. Dehydrated powdered maca root contains 8.87–11.6% protein, 1.09–2.2% lipid, 54.6–60.0% carbohydrate (23.4% sucrose, 1.55% glucose, 4.56% oligosaccharides, 30.4% polysaccharides), 8.23–9.08% fibre, 4.9–5.0% ash, and an energy content of 663 kJ/100 g (Dini, Migliuolo, Rastrelli, Saturnine, & Schettino, 1994; Yu & Jin, 2004; Valentová et al., 2006). There are 18 or 19 kinds of amino acid in maca root. Among them seven essential amino acids (Trp is under- treated) are found, and their content (342.6–388.6 mg/g protein) is higher than those in potatoes and carrots. The content of unsaturated fatty acids, such as linoleic and oleic, is 52.7–60.3% of total fatty acids, which shows a good composition of unsaturated compounds. The maca root powder is also abundant in minerals (Dini et al., 1994; Yu & Jin, 2004). The mineral contents of maca reported in Dini et al. (1994) were Fe 16.6, Mn 0.8, Cu 5.9, Zn 3.8, Na 18.7, K 2050 and Ca 150 (mg/100 g dry matter).

2.1. Macaene and macamide

Many kinds of secondary metabolites have been found in maca root. The typical markers for maca are macaene and macamide, the novel polyunsaturated fatty acids and their amides which are not found in other plants (Ganzera, Zhao, Muhammad, & Khan, 2002; McCollom, Villinski, McPhail, Craker, & Gafner, 2005; Muhammad, Zhao, Dunbar, & Khan, 2002; Zhao, Muhammad, Dunbar, Mustafa, & Khan, 2005). It has been proposed that macaene and macamide be the group of biologically active components in maca involved in improving sexual performance (Zheng et al., 2000). The contents of these unusual compounds vary widely in different maca samples. In dried maca, macaene ranges from around 0.09–0.45%, and macamide ranges from 0.06% to 0.52% (Ganzera et al., 2002). One macaene and sixteen types of macamide have been found up to now. The structures of macaene and macamides are shown in Figs. 1 and 2, respectively.

2.2. Glucosinolates and their derivatives

Glucosinolates, and their derived products, have received significant scientific attention because of their...
biological activities, in particular their ability to combat pathogens and cancer (Fahey, Zalcman, & Talalay, 2001). They are widely distributed in cruciferous crops, and are considered largely responsible for the distinctive, pungent flavor of maca. There are nine kinds of glucosinolates found in maca. Most are aromatic glucosinolates (Dini, Tenore, & Dini, 2002; Flores et al., 2003; Li, Ammermann, & Quiros, 2001; Piacente, Carbone, Plaza, Zampelli, & Pizza, 2002). The structures of these maca glucosinolates are shown in Fig. 3. The content of glucosinolates in fresh maca is about 1% which is about 100 times that found in cruciferous crops such as cabbage, cauliflower and broccoli (Li et al., 2001). The content and type of glucosinolates in maca present vary in different organs of the plant, such as seeds, sprouts, but also varies according to plant age. In maca, the total content of glucosinolates is highest in fresh hypocotyls, followed by the seeds, sprouts, then dried hypocotyls, and fresh leaves (Li et al., 2001). Glucosinolate can be hydrolyzed to a series of different compounds, such as isothiocyanate, thiocyanate and nitriles by the endogenous enzyme, myrosinase (Fig. 4) (Fahey et al., 2001). In the intact cells, glucosinolates are separated from myrosinase. However, when the cells are damaged, glucosinolates can be easily broken down by this enzyme. This is the main reason why dried maca roots or processed products have much lower glucosinolates content than fresh tissue and seeds (Li et al., 2001; Piacente et al., 2002).

2.3. Alkaloids

Alkaloids are mainly found in nature amongst the members of the plant kingdom, though some fungi also naturally secrete these compounds. They are generally classified into about 60 different kinds according to their basic structures. Most alkaloids show some form of biological activities. Three alkaloids have been isolated from maca roots: two imidazole alkaloids (lepidiline A and lepidiline B) (Cui, Zheng, He, & Zheng, 2003) and one benzylated derivative of 1,2-dihydro-3-hydroxypyridine (macaridine) (Muhammad et al., 2002). Their structures are shown in Fig. 5.

2.4. Sterols

Many types of phytosterols have been isolated from maca (Dini et al., 1994; Zheng et al., 2000). Phytosterols are bioactive compounds found in all vegetable foods. In plants, more than 200 different types of phytosterols have been reported. The most abundant types are β-sitosterol, campesterol and stigmasterol. These compounds are not only potent reducers of plasma cholesterol levels, but also
exhibit anti-cancer, anti-inflammatory and anti-oxidant properties (Lagarda, García-Llatas, & Farré, 2006). The structures of the phytosterols found in maca are shown in Fig. 6.

2.3. Other compounds

1R,3S-1-methyltetrahydro-β-carboline-3-carboxylic acid, a compound which can act as an inhibitor of the enzyme monoamine oxidase, has been identified in maca. Its structure is shown in Fig. 7 (Piacente et al., 2002). Monoamine oxidase inhibitors (MOAI), which inhibit monoamine oxidation, are mainly used in psychiatry for the treatment of depressive disorders, and in neurology for the alleviation of the symptoms of Parkinson’s disease (Volz & Gleiter, 1998). Some foods for which individuals often express cravings, such as chocolate and cocoa, also contain these compounds, and the presence of these compounds in such foodstuffs has been hypothesized to play a role in craving (Piacente et al., 2002).

3. The biological activities of maca

3.1. Improving fertility

In the formation of the Inca Empire, maca was used to improve fertilities of both humans and their livestock. This was thought to be essential because fertility rates were generally considered to be much weakened at high altitude (Quiros & Cárdenas, 1992). Now the effects of maca have been scientifically examined using the rat model. Administration of maca was found to prevent the reduction in both body weight and epididymal sperm count induced by high altitude (Gonzales et al., 2004), and also to reduce the deleterious effect of malathion or lead acetate on spermatogenesis in rats (Bustos-Obregón, Yucra, & Gonzales, 2005; Rubio et al., 2006a). Meanwhile normal male rats treated with maca extracts showed significantly increased epididymal sperm counts and spermatids, and higher testicular and epididymis weights (Gonzales, Ruiz, Gonzales, Villegas, & Córdova, 2001a). These effects were dose-dependent (Chung, Rubio, Gonzales, Gasco, & Gonzales, 2005; Gonzales et al., 2004). Trans-illumination in freshly isolated unstained seminiferous tubules has been used to detect changes in the lengths of seminiferous epithelium stages in male rats after oral administration of maca. The results showed that maca significantly increased spermatogenesis in rats (Bustos-Obregón et al., 2005; Chung et al., 2005; Gonzales et al., 2001a, 2004; Rubio et al., 2006a). Maca has been shown to have the same effects in humans. It was found that oral administration of maca tablets to normal adult men over a period of 4 months, led to seminal volume increasing from 2.23 ml to 2.91 ml, sperm count per ejaculum increased from 140.95 $\times$ 10^6/ml to 259.29 $\times$ 10^6/ml, while motile sperm count increased from 87.72 $\times$ 10^6/ml to 183.16 $\times$ 10^6/ml. These semen variables following the oral administration of maca for the period of 4 months were significantly different from those on the test group prior to administration (Gonzales et al., 2001b).

Maca has also been shown to improve the fertility in females. Oral administration of maca extract to mice, led to increased litter size and pregnancy rates in adult female mice (Kuo, Chang, & Liau, 2003; Menaldo, Serrano, & Lopez, 2001; Ruiz-Luna et al., 2005).

The mechanism of maca improving fertility of male and female is not yet fully elucidated. Some studies have shown that maca extracts exhibited estrogenic activity, which led MCF-7 cells, a estrogen-positive cell line, to proliferate in vitro (Valentová et al., 2006), and also to increased uterine weight in rats (Rubio, Caldas, Dacila, Gasco, &
The effects of estrogenic activity of maca may be partly due to the content of phytosterols in the extracts (Moreau, Whitaker, & Hicks, 2002). This estrogenic activity of maca may help explain the means by which it improves female fertility. Earlier studies showed that the role of estrogens in both spermatogenesis and sexual desire in man is complex. Estrogens are important to males as well as to females and they have been proposed that they should be considered as ‘male hormones’ (O’Donnell, Robertson, Jones, & Simpson, 2001).

However, other studies take the view that maca does not act in a hormone-like fashion to improve fertility. This conclusion is based on the following findings:

1. Following administration of maca extracts, serum levels of reproductive hormones such as luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin (PRL), testosterone (T) and estradiol (E2) are not modified (Chung et al., 2005; Gonzales et al., 2001b, 2003a, 2003b, 2005, 2006).
The weights of androgen-dependent organs (except for the epididymis), such as the seminal vesicles and the prostate, are unaffected by oral administration of maca. The reason for the increased epididymal weights noted may be due to an increase in sperm number (Gonzales et al., 2001a, 2001b, 2003a), and to the fact that the seminal vesicles are more sensitive to androgens than the other two organs. 

Macaca extracts could not activate human androgen receptors, and this therefore excluded a direct effect of maca on genes regulated by androgens (Bogani et al., 2006).

Therefore, the subject of whether or not the estrogenic activity of maca plays an important role in altering fertility in man clearly needs further attention.

### 3.2. Improving sexual performance

Within the Andean region maca is widely held in high repute as an aphrodisiac for both men and women. Rat and mouse models have been used to assess the validity of this claimed effect. It was found that oral administration of maca.

![Fig. 5. The structures of alkaloids found in maca.](image1)

![Fig. 6. The structures of phytosterols found in maca.](image2)
of maca extracts improved the copulatory performance of sexually inexperienced male mice or rats (Cicero, Bandieri, & Arletti, 2001, 2002). Additionally, administration of maca improved the erectile function and decreased the latent period of erection of testes-removed rats (Zheng et al., 2000). Double-blind, placebo-controlled, randomized, parallel trials carried out on men have reported a widespread increase in sexual desire in the test group (Gonzales et al., 2002, 2003b). In the study of Gonzales et al. (2002), 56 (21–56-year-old) healthy men took part in the trial, and their sexual desire was assessed using a subjective (self-reporting) measure. The result showed the percentage of the men manifesting increased sexual desire was 40.0% and 42.2% after 8 and 12 weeks, respectively of maca treatment, which was significantly different from the results in the placebo-treated groups. But by contrast, results obtained by Roberts, Jean, Berman, and Padmanyatham (2001) showed that maca did not affect penile blood flow in men with mild-to-moderate erectile dysfunction. Further larger scale studies on men are needed to assess the role(s) of maca.

The mechanisms of maca’s proposed improvement of sexual performance have been studied, but have not been fully clarified so far. Test results have shown that maca’s effect on fertility and sexual desire may not act by modulation of the hypothalamic–pituitary axis to regulate hormone secretion (Bogani et al., 2006; Gonzales et al., 2002, 2003a, 2003b), and was also independent of changes in scores for depression and anxiety (Gonzales et al., 2002). Meanwhile, during oral administration of maca to mice, the apparent absence of correlation between effect on spontaneous motility and sexual behavior, seemed to support the hypothesis that maca had a pharmacological action independent of its nutritional value (Cicero et al., 2001). Maca was also found not to activate the human androgen receptors and thus not to influence genes regulated by androgens (Bogani et al., 2006). There is clearly a need for further studies in this area to resolve some of these apparent contradictions.

3.3. Anti-proliferative function

Maca has anti-proliferative functions, and may mitigate the prostate weight increase induced by testosterone treatment (Gonzales et al., 2006, 2005). The mechanism of this anti-proliferative function may include:

1. Maca has ability to scavenge free radicals, and provide cytoprotection under oxidative stress conditions (Lee, Dabrowski, Sandoval, & Miller, 2005; Sandoval et al., 2002). Research has shown that reactive oxygen and nitrogen species (ROS/RNS) (superoxide, hydroxyl, peroxyl, H2O2 and peroxynitrite) are implicated in the etiology of degenerative diseases, including cardiovascular disease, diabetes, cancer, neurodegenerative disorders, and aging. Maca scavenges ROS/RNS, and thus helps protect cells from pathological changes.

2. Many studies have shown that consumption of cruciferous vegetables reduces the risk of many types of cancer. The chemoprotective activity of these vegetables is widely believed to be due to their content of minor dietary components, such as glucosinolates and their derivatives. It was reported that glucosinolates and their derivatives had potential anti-proliferative and cancer-preventive properties (Fahey et al., 2001). The content of glucosinolates in fresh maca is about 1%, which is about 100 times more than those in other cruciferous crops. Thus, by logical argument, it is proposed that the unusually high content of glucosinolates and derivatives, endow maca with more potent anti-cancer capabilities.

3. The alkaloids and sterols present in maca may also contribute to its proposed anti-cancer activity. Cui et al. (2003) reported that both Lepidiline A and B had selectively cytotoxic activities against some human cancer cells. Likewise, the potential anti-cancer activity of phytosterols has been previously noted (Lagarda et al., 2006).

3.4. Role in vitality and stress tolerance

Administration of maca can reduce the effects of stress, including combating the increase in corticosterone and all the parameters related to this increase, such as the size of adrenal glands and the stress-induced ulcers, and eliminate the decrease in free fatty-acids and glucose levels in plasma, produced by stress (López-Fando, Gómez-Serranillos, Lock, Upamayt, & Carretero, 2004). Maca powder has also been shown to exhibit an anti-tiredness effect, and can increase the duration of mobility in forced swimming tests of mice (López-Fando et al., 2004; Rubio et al., 2006b; Yu & Jin, 2004).

Maca is abundant in protein, unsaturated fatty acids and minerals. Its highly nutritious nature is proposed as one reason for its effect on vitality and combating tiredness. The reason behind maca’s mitigation of stress effects is unclear. It is hypothesized that maca may lead to activation of the hypothalamic–pituitary–adrenal axis to increase adaptogens, and by this means increase generalized resistance to various noxious and stressful stimuli (López-Fando et al., 2004).
3.5. Improving growth rate

Maca meal supplementation increased food intake, growth and feed utilization along with improving survival in rainbow trout juveniles (Lee et al., 2004, 2005). The improvement in survival might be explained via maca stimulating growth hormone and imparting increased resistance to diseases or stresses. First, it has been widely shown that maca contains many kinds of sterol, which have estrogenic effects (Moreau et al., 2002), and previous studies have shown that estrogen promoted the growth of yellow perch and production of growth hormone in goldfish (Lee et al., 2005). Secondly, maca improves immunity by increasing leucocyte number (Lee et al., 2004). Thirdly, anti-oxidant activity in maca meal may be partly responsible for the increased immunity and resistance to pathological antigens in the rainbow trout alevins and juveniles (Lee et al., 2004). Fourthly, maca is a good nurture which is abundant in protein, unsaturated fatty acid, vitamins and minerals.

3.6. Anti-postmenopausal osteoporosis

The onset of the menopause symptoms is generally linked with reduced concentrations of the female sex hormones. One of the consequences of this is reduction of bone mineral density. Maca is said to regulate incretion, and has been used to treat women with menopausal symptoms. Studies in ovariectomized rats have shown that maca significantly increased calcium content in the femur of the rats (Zhang et al., 2006). The mechanism by which maca protects ovariectomized rat against osteoporosis is different from that of hormone replacement therapy (HRT). Maca did not significantly increase estrogen levels and uterine weights (Chung et al., 2005; Gonzales et al., 2001a, 2003a, 2005; Zhang et al., 2006), and had less side-effects than HRT. Maca also exhibited no significant effect on bone metabolic markers in serum and other biochemical parameters, and thus at the levels used did not participate in the bone metabolism (Zhang et al., 2006). Phytoestrogens and other secondary metabolites in maca may contribute to this function.

4. Toxicity

Maca may have low toxicity to some biological systems (Valerio & Gonzales, 2005). e.g. oil of maca (100 μg/ml) is said to be selectively toxic to the cyanobacterium Oscillato- ria perpernata, and at 1% (w/w), maca oil also appeared to act as a feeding deterrent to termites (Tellez et al., 2002). Most researchers dispute this opinion. It was reported that people usually eat about 50–100 g dry maca per meal (0.71–1.42 g of dry roots per kg of body weight) (Chung et al., 2005). However, following oral administration of maca to rats at normal to high dose, equal to 10 times the normal human rate of consumption, the body weights and organs of rats, showed no measurable difference from the controls (Chung et al., 2005; Gonzales et al., 2006). The results showed that maca had no toxicity to animals. On the contrary, Valentová et al. (2006) found that maca exhibited a slight cytoprotective effect in live animals.

5. Different nutritional contents and biological effects according to maca ecotype

The nutritional contents and pharmacological functions of maca are different according to their color. Maca has eight or more ecotypes according to the colors of its hypocotyls (Rea, 1994). Red maca has a higher content of pure protein and potassium, and lower content of soluble sugars, riboflavin, and iron than black maca, whereas yellow maca has intermediate values for these compounds (Yllescas, 1994). The infrared spectra of lyophilized aqueous extracts of red, yellow and black maca showed seven peaks with different absorbances. Among them, red maca had the highest peak values, followed by yellow maca and black maca (Gonzales et al., 2005). Thus, it is likely that different biological activities will be observed when different ecotypes are used in studies. For example, red maca, but neither yellow nor black maca, has anti-proliferative functions reducing ventral prostate size, and prevents the prostate weight increase induced by testosterone treatment in rats (Bogani et al., 2006; Gonzales et al., 2005, 2006). Black and yellow maca increased spermatic counts in testis and sperm counts in the epididymis, while red maca did not have this effect. Among the three ecotypes, the best reproductive effect is observed with black maca, followed by yellow maca, and then red maca (Gonzales et al., 2006).

6. Outlook

Sexual function is an important component of human life quality and subjective well being. Sexual problems, which are mainly related to sexual desire and male erectile dysfunction, are extremely prevalent among both men and women (Gonzales et al., 2002; Laumann, Paik, & Rosen, 1999). It is stated that 10–52% of men and 25–63% of women are suffering from sexual dysfunction in USA (Tharakan & Manyam, 2005). Testosterone is used to stimulate sexual desire in hypogonadal men, but it should not be used in men with normal serum testosterone levels. Meanwhile, testosterone may be a promoter of prostate cancer (Gonzales et al., 2003a). As well as Viagra, a successful drug to moderate erectile dysfunction, some natural products with erectile-dysfunction activity are attracting the attention of the scientific community now. Maca is one of these (Drewes, George, & Khan, 2003; Tharakan & Manyam, 2005). Maca has some advantages over testosterone and Viagra in improving sexual function: (1) Maca improves sexual performance without changing serum reproductive hormone level, thus reducing the risk of stimulating prostate cancer associated with testosterone therapy. (2) Oral administration of maca increased sexual desire in normal males as well as in those with erectile dysfunction. (3) Maca...
administration has far fewer and less serious side effects than testosterone and Viagra. (4) Maca consumption is generally beneficial to both men and women. The increased public belief in the potential benefits of “natural” medicines, the public reticence to discuss difficulties in this area, and the ability to initiate and control one’s own therapeutic regime without recourse to medical professionals, mean that maca may well be used in parallel with the current standard medications in improving sexual function. A direct comparison could be drawn is the use of St. John’s Wort by many Europeans to help combat mild to moderate depression, as an effective alternative (at least as far as the general public are concerned) to conventional anti-depressants such as selective serotonin re-uptake inhibitors, generally only available via medical professionals.

Lots of postmenopausal women suffer from menopause symptoms. Menopause symptoms are generally linked with reduced circulating concentrations of female sex hormones, and may be associated with mood changes, decreased libido, poor quality of life and reduced bone mineral density. Hormone replacement therapy (HRT) has proven efficacious in alleviating symptoms and diseases in postmenopausal women. But the findings from the Women’s Health Initiative Trial, suggest that long-term HRT use increases the risk of breast cancer, endometrial cancer, thromboembolic events and vaginal bleeding. It is said that overall health risks exceed benefits from HRT (Rossouw et al., 2002). Maca can alleviate menopause symptoms without changing serum hormone levels, which may offer an alternative therapy to HRT for post-menopausal woman.

Although many studies have been carried out into maca, the effective substances within it and the mechanisms of action of maca have not been fully elucidated as yet. Given the promise it holds out, and the wealth of subjective evidence, this plant’s activities need much more intense scrutiny in the future, focusing on both factors affecting composition, and the relationship between this and its pharmacological activities.

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