



Lepidium meyenii (Maca) enhances the serum levels of luteinising hormone in female rats

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11198769)

N-benzyloctadecanamide (PubChem CID:

220495)

(9Z,12Z)-N-benzyloctadeca-9,12-dienamide

(PubChem CID: 68742556)

Linoleic Acid (PubChem CID: 3931)

alpha-Linolenic Acid (PubChem CID:

5280934)

ABSTRACT

Ethnopharmacological relevance: *Lepidium meyenii* (Maca) is traditionally employed in the Andean region for its supposed fertility benefits. This study investigated the effect of Maca on the serum pituitary hormone levels during the pro-oestrus phase.

Materials and methods: Maca powder was made from the tubers of *Lepidium meyenii* Walp collected, dried, and reduced to powder at the plantation in Junín Plateau and was purchased from Yamano del Perú SAC. The Maca powder was identified by chemical profiling and taxonomic methods. Two groups of female Sprague-Dawley rats were provided feed with normal feed containing 5%, 25%, or 50% Maca powder *ad libitum* for 7 weeks. At 1800 h of the proestrus stage, the rats were euthanised, and blood samples were collected for serum isolation. The serum pituitary hormone levels were measured using enzyme-linked immunosorbent assays (ELISAs).

Results: No significant differences in feed intake or growth rate were observed among the rats. During the pro-oestrus stage, a 4.5-fold increase ($P < 0.01$) in luteinising hormone (LH) and a 19-fold increase ($P < 0.01$) in follicle-stimulating hormone (FSH) were observed in the sera of rats fed with 50% Maca powder compared with the control rats. No significant differences were observed in the levels of the other pituitary hormones, including growth hormone (GH), prolactin (PRL), adrenocorticotrophic hormone (ACTH), and thyroid-stimulating hormone (TSH). A dose-dependent increase of LH serum levels was observed within the range of 3–30 g Maca/kg. Furthermore, the enhancement of the LH serum levels was specific to the pro-oestrus LH surge.

Conclusions: The present study demonstrates that Maca uniquely enhances the LH serum levels of pituitary hormones in female rats during the pro-oestrus LH surge and acts in a pharmacological, dose-dependent manner. These findings support the traditional use of Maca to enhance fertility and suggest a potential molecular mechanism responsible for its effects.

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1. Introduction

Lepidium meyenii is an herbaceous biennial plant of the Brassicaceae family that is native to the high Andes of Peru. Peruvians have used the root of *Lepidium meyenii*, known as Maca, for centuries as both a nutritious food and fertility medicine for humans and animals. In randomised clinical trials, Maca showed a positive effect on mild erectile dysfunction (Zenico et al., 2009), and it has been shown to improve sexual desire in healthy menopausal women (Brooks et al., 2008). These studies provide preliminary evidence supporting the effectiveness of Maca (Shin et al., 2010). Biological and pharmacological studies of Maca using animal

models have reported various health-related properties, such as a fertility-increasing effect (Ruiz-Luna et al., 2005) and positive effects on sexual performance (Cicero et al., 2001; Zheng et al., 2000), spermatogenesis (Chung et al., 2005; Gonzales et al., 2004, 2006), osteoporosis (Zhang et al., 2006), neuronal function (Pino-Figueroa et al., 2010), memory impairment (Rubio et al., 2006a, 2007, 2011), chemical and physical stress responses (Gonzales-Castaneda et al., 2011; Lopez-Fando et al., 2004; Rubio et al., 2006b), prostatic hyperplasia (Gasco et al., 2007), and locomotion (Cicero et al., 2001).

Fertility is based on the physiology of the hypothalamic-pituitary-gonadal (HPG) axis. A pro-oestrus LH surge from the anterior pituitary triggers ovulation and the development of the corpus luteum, which is required for fertility. The hormone level of the proestrus LH surge is influenced by genetic background, environment, and physical condition. Traditionally, Maca has been used to promote fertility in a harsh environment, at an altitude over 4000 m. However, no significant alterations in the serum

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levels of pituitary hormones containing LH were detected in previous studies using Maca or its ingredients (Gonzales et al., 2009); therefore, the molecular mechanism of the effect of Maca cannot be accessed via its target proteins.

The present study investigated the effect of Maca on the LH serum levels during the LH surge in female rats.

2. Materials and methods

2.1. Plant material

Lepidium meyenii Walp was harvested from the Junín Plateau area (the Central Andean Region of Peru at altitudes between 4200 and 4500 m) in 2010. The tubers of *Lepidium meyenii* were collected, dried, reduced to powder at the plantation in Junín Plateau, and made commercially available as Maca. The Maca powder was purchased from Yamano del Perú SAC.

A voucher specimen (MG-2A/YDP-S002-2011) was deposited at the San Marcos University Natural History Museum's herbarium where the powder was identified as *Lepidium meyenii* Walp with a taxonomic position based on the Cronquist classification method by Dr. Betty Millán Salazar.

2.2. Solvents and chemicals

Acetonitrile, EDTA dipotassium salt (EDTA-2K), petroleum ether, and trifluoroacetic acid were purchased from Wako Pure Chemicals (Osaka, Japan).

2.3. The preparation of Maca petroleum ether extracts

The Maca powder was extracted using petroleum ether based on the method employed by McCollom and colleagues (McCollom et al., 2005). A 10.0-g portion of dried Maca was extracted using 50 ml of petroleum ether by incubating it at 20 °C for 24 h, shaken at 150 rpm. After filtration, the supernatants were evaporated, providing 43.0 mg of residue. The residue was resolved using 1 ml of acetonitrile. Prior to the HPLC-UV-MS/MS analysis, all samples were filtered using a 0.45- μ m PTFE syringe filter from Millipore.

2.4. Analytical HPLC

The HPLC experiments were performed using a Shimadzu LC-30A HPLC system equipped with a UV-vis detector. The macamides were qualitatively and quantitatively analysed using an Inertsil ODS-3 column (250 $\times$ 4.6 mm² id, 5- μ m particle size; GL Sciences, Tokyo, Japan). The solvent system consisted of (A) water with 0.005% trifluoroacetic acid and (B) acetonitrile with 0.005% trifluoroacetic acid using a gradient of 20:80 (A:B) to 0:100 over 24 min. The flow rate was set at 0.8 ml/min. The column oven was set to 40 °C, and 5 μ l of sample was injected. The macamides were relatively quantified using peak area calculations at detection wavelengths of 210 nm and 280 nm. The macamides were qualitatively analysed by comparing the retention times, UV/vis-spectra ratio, and MS analysis with the data reported for authentic samples (Ganzera et al., 2002; McCollom et al., 2005).

2.5. The MS/MS analysis of macamides

A HPLC-MS/MS system consisting of a Shimadzu LC-30A HPLC system equipped with an automatic sample injector, bi-pump, UV-vis detector, and a Thermo Fisher Scientific series Q-Exactive MS/MS (Yokohama, Japan) was used with the following parameters: high voltage capillary, 4500 V; capillary exit, 143.6 V; skimmer 1, 31.1 V; trap drive, 44.2; scan range (m/z), 150–800. The mass

spectrometer was operated in positive ion detection mode. The HPLC conditions applied in the MS/MS analysis were identical to those used for the analytical HPLC.

2.6. Feed and animals

CE2 laboratory chow was purchased from CLEA Inc. (Fukuoka, Japan) and used as the control feed. The 5%, 25%, and 50% Maca feed were prepared by adding 5%, 25%, and 50% (w/w) Maca powder to CE2, respectively, and swirling the mixture 100 times in a nylon bag. The CE2 and Maca powder were stored at room temperature.

Two-week-old female Sprague-Dawley rats (Charles River Laboratories, Tokyo, Japan) were purchased from Oriental Yeast Co., Ltd. (Tokyo, Japan) and kept for 8 weeks in the animal facility at Nakamura Gakuen University. The rats were maintained individually in stainless-steel wire-mesh cages at room temperature (25 °C) with a 12-h light/12-h dark cycle (0600 h/1800 h). The rats were provided with feed and tap water *ad libitum* and bred for 7 weeks. The Animal Ethics Committee of Nakamura Gakuen University approved the animal manipulations described in this paper.

The rats were habituated to the animal facility for 1 week prior to the start of the experiments. The rats were randomly divided into three test groups and one control group: the first group received 5% Maca feed ($n=10$ rats), the second received 25% Maca feed ($n=10$ rats), the third received 50% Maca feed ($n=20$ rats), and the fourth received the control feed ($n=20$ rats). Body weight and feed intake were monitored every other day from 0815 h to 0900 h for 7 weeks. The residual feed was weighed every other day. The feed intake was calculated by subtracting the residual feed from the total feed. Feed efficiency was indexed as feed intake (g)/body weight (kg).

2.7. Oestrous cycle

The oestrous cycle was monitored via vaginal smears taken daily for 2 weeks. Each vaginal smear was taken between 0830 h and 0900 h. The smears were stained with Giemsa Stain Solution (Merck Japan Ltd., Osaka, Japan) for microscopic examination. Oestrus was characterised using the ratio of the number of nucleated epithelial cells to the number of cornified cells. The numbers of nucleated epithelial and cornified cells were determined under a microscope using a Burkert-Türk haemocytometer. Blood samples were obtained from the rats that displayed 4-day oestrous cycles based on this criterion.

2.8. Euthanasia and sampling

All samples were obtained via decapitation at 1630 h or 1800 $\pm$ 15 h during the pro-oestrus stage. Trunk blood was collected into tubes with or without EDTA-2K and then centrifuged at 3000 rpm for 10 min. The resulting serum and plasma were stored at -80 °C for subsequent analyses. The organs were dissected free of fat and weighed.

2.9. Hormone assays

The serum concentrations of LH, FSH, GH, and TSH were measured using enzyme-linked immunosorbent assay (ELISA) with the Libs[®] Rat LH ELISA kit, Libs[®] Rat FSH ELISA kit, Libs[®] Rat GH ELISA kit, and Libs[®] Rat TSH ELISA kit (Shibayagi Co., Ltd., Gunma, Japan), respectively. PRL serum concentration was measured using enzyme immunoassay (EIA) with the Pana-test[®] Rat PRL EIA kit (Panapharm Laboratories Co., Ltd., Kumamoto, Japan). ACTH plasma concentration was measured using chemiluminescence enzyme immunoassay (CLEIA) with the Siemens-Immulyze[®] ACTH II (Siemens Healthcare

Diagnostics K. K., Tokyo, Japan). All procedures were performed according to the manufacturer's instructions.

2.10. Data analyses

The data are presented as the mean $\pm$ standard deviation (SD) and analysed using a one-way analysis of variance followed by Student's *t*-tests for two-group comparisons using IBM SPSS (Statistical Package for the Social Sciences) Version 19 (IBM Japan Ltd., Tokyo, Japan). A value of $p < 0.01$ was considered significant.

3. Results

3.1. Maca quality assessment via chemical profiling

Macamides are a distinct class of secondary metabolites and useful marker compounds for the quality control of *Lepidium meyenii* products (Ganzera et al., 2002; McCollom et al., 2005). We extracted Maca powder with petroleum ether to give a yield of 0.460% w/w and performed an HPLC-UV-MS analysis. The molecular ion peaks in the mass spectra, comparative retention times, and UV-vis ratios for twelve macamides detected in the extracts (Table 1) were identical to those in the chemical profile reports of *Lepidium meyenii* Walp (Ganzera et al., 2002; McCollom et al., 2005). To confirm the identification of the macamides, we detected fragment ion peaks from the macamides via MS/MS analysis. The individual fragments of *m/z* 91.05 and *m/z* 121.06 were detected as corresponding to benzyl ions ($C_7H_7^+$) and methoxybenzyl ions ($C_8H_9O^+$) from seven and five macamides, respectively (Table 1). The major components of the extract were linoleic acid and linolenic acid, which was initially determined by MS analysis (Table 1). These results demonstrate that the Maca powder used could be chemically identified as the tubers of *Lepidium meyenii* Walp and using the plant taxonomy described in the experimental section.

3.2. General observations in the rat experiments

Significant differences were not observed in the intake of feed with or without Maca powder (Fig. 1a) or the growth rate (Fig. 1b) of the rats throughout the study. The feed intake was constant at 15 g/day after 38 days of age and could be used in experiments of the Maca dose-response relationship. Moreover, significant differences were not observed between the test and control groups with regard to the organ weights of the ovary, uterus, hypothalamus, pituitary gland (Table 2), or other organs (data not shown). Maca intake did not significantly alter the weights of the HPG axis organs.

Because circadian rhythm (McCormack and Sridaran, 1978), ovulation cycle (Cooper et al., 1980), and stress (Krulich et al., 1974) strongly influence LH secretion, the sample collection was strictly controlled under a time course based on ovulation. The time of ovulation was determined by vaginal smears. All rats used showed a pattern characteristic of a typical 4-day oestrus cycle (Fig. 2).

3.3. The effect of Maca on serum pituitary hormone levels during LH surge

The 4-day oestrus cycle was subdivided into pro-oestrus, oestrus, metoestrus, and dioestrus (Fig. 2). Because the maximum concentration of LH in the preovulatory LH surge occurs at 1800 h of the pro-oestrus stage (Cooper et al., 1980), the rat sera were collected at 1800 ± 15 h of the pro-oestrus stage. The rat sera were analysed for pituitary hormones using ELISA. The serum levels of LH (22.1 ng/ml vs. 4.9 ng/ml, $p < 0.001$) and FSH (9.5 ng/ml versus

0.5 ng/ml, $p < 0.01$) significantly increased among the test group of rats fed with 50% Maca powder compared with the control group (Table 3). The other pituitary hormones, GH, ACTH, TSH, and PRL, did not show significant differences between the test and control groups (Table 3). These results showed that the LH serum levels exhibited a 4.5-fold increase ($p < 0.001$) in the pro-oestrus stage after feeding with the 50% Maca powder in female rats.

The vaginal smear test indicated that ovulation was the same across the normal 4-day oestrus cycle in the test and control groups. Because the timing of the LH surge is critical for ovulation, we investigated the timing of the LH enhancement and subsequent FSH after Maca intake. The initiation time of the LH surge was measured using serum collected before 1800 h in the pro-oestrus stage. The initiation of the LH surge showed the same pattern in the test and control groups, with the LH serum levels beginning to elevate at 1730 h (Fig. 3). Therefore, no significant between-group differences were observed in the initiation time of the LH surge. Because the FSH serum levels presumably represent the initial phase according to the HPG axis pathway (Butcher et al., 1974), the rats fed with 50% Maca powder showed an FSH elevation at the same time as those in the control group (Fig. 3). These results demonstrate that Maca intake can enhance LH serum levels among the pituitary hormones with respect to the timing of a normal LH surge pattern.

The production of LH involves different mechanisms between the LH surge and pulsate phases. The LH increase in the LH pulsate phase is associated with menopause and not with an improvement in triggering ovulation. To investigate the effect of Maca on the LH pulsate phase, blood was collected at 1630 h in the pro-oestrus stage. The LH concentration in the blood was determined. The results were used to compare the LH serum levels obtained at different blood collection times (Fig. 4). The time of 1630 h in the pro-oestrus stage represented the LH pulsate phase because the LH serum levels in the control group were low (1.8 ng/ml) but elevated approximately 1 h later (6.6 ng/ml, $p < 0.01$; Cooper et al., 1980). Significant differences were not observed between the test (2.2 ng/ml) and control (1.8 ng/ml) groups with regard to the LH serum levels in the LH pulsate phase (Fig. 4). These results show that the LH-enhancing effect due to Maca intake is a specific action regarding the timing of the LH surge and normal physiological processes in the HPG axis.

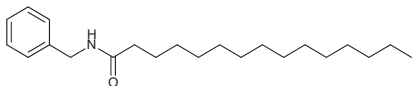
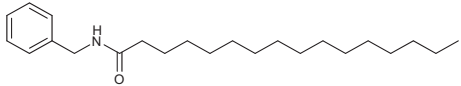
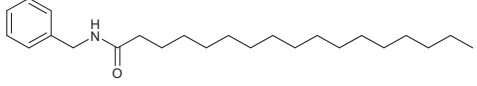
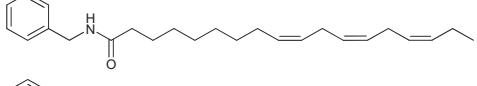
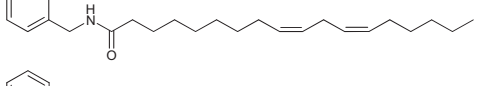
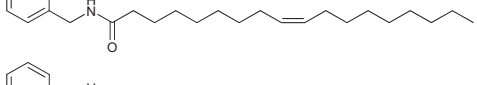
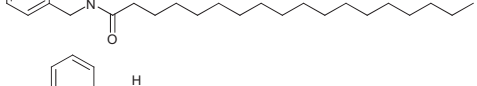
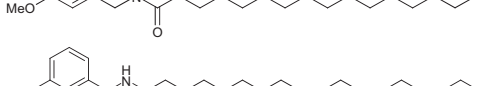
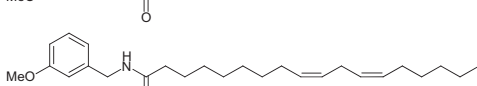
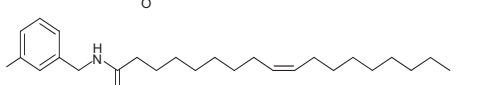
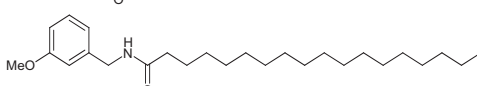
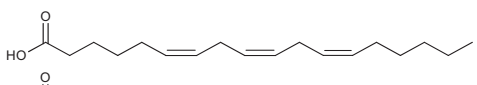
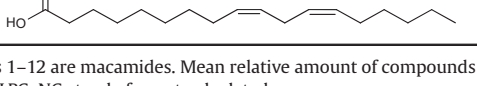
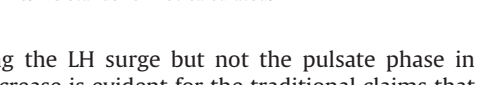
3.4. Dose-response of the LH-enhancing effect

To evaluate the dose-response relationship of the increase in LH serum levels, rats were fed with feed containing 5%, 25%, or 50% Maca powder. Because the amount of feed intake was constant across all rats older than 38 days (Fig. 1A), each concentration of Maca powder in the feed corresponded to an oral administration of 3.0, 15, or 30 g of Maca/kg weight, respectively. Sera were collected from 10-week-old rats at 1800 ± 15 h in the proestrus stage, and the LH concentrations in the sera were subsequently measured via ELISA. The results revealed a dose-dependent relationship between LH serum levels and amount of Maca intake (Fig. 5). The LH-enhancing effect in the serum was sustained at an intake of greater than 15 g Maca/kg/day, which corresponded to feeding with 25% Maca *ad libitum*.

4. Discussion

Previous studies of Maca have successfully identified its various health-promoting activities (Gonzales, 2012). However, previous experiments had not found an alteration of the LH serum levels, which play a key role in fertility through the HPG axis. The present study is the first to demonstrate that Maca intake enhances LH

Table 1
Chemical profiling of macamides identified by HPLC-UV-MS/MS analysis of extracts of the Maca powder.

Compound Number	Identified Chemical Structure	Retention Time (min.)	[M-H] ⁺	Main Fragment Ions	Relative amount (%)	CV%
1		15.8	332.3	MS ² [332.3]: 91.1	0.19	11.2
2		18.2	346.3	MS ² [346.3]: 91.1	13.56	4.4
3		20.8	360.3	MS ² [360.3]: 91.1	0.10	10.8
4		12.4	368.3	MS ² [368.3]: 91.1	4.73	5.7
5		15.2	370.3	MS ² [370.3]: 91.1	5.73	0.8
6		18.7	372.3	MS ² [372.3]: 91.1	2.28	8.3
7		23.4	374.3	MS ² [374.3]: 91.1	3.37	9.7
8		17.6	376.3	MS ² [376.3]: 121.1	4.82	4.3
9		12	398.3	MS ² [398.3]: 91.1, 121.1	0.82	7.9
10		14.7	400.3	MS ² [400.3]: 91.1, 121.1	0.46	3.1
11		18.1	402.3	MS ² [402.3]: 91.1, 121.1	< 0.10	NC
12		22.6	404.4	MS ² [404.4]: 91.1, 121.1	3.37	3.5
13		10.3	279.2		35.40	1.5
14		12.9	281.2		25.16	1.3

The compound numbers 1–12 are macamides. Mean relative amount of compounds in the extracts and coefficient of variation (CV) are shown with the percentage (%) in four tests of the analytical HPLC. NC stands for not calculated.

serum levels during the LH surge but not the pulsate phase in female rats. This increase is evident for the traditional claims that Maca is an aphrodisiac in enhancing sexual drive and female fertility in humans and domestic animals.

Clinical studies of the effects of Maca on sexual function have investigated low doses of up to 3.5 g/day of Maca (Gonzales et al., 2003; Meissner et al., 2006b; Shin et al., 2010). In those doses, Maca did not affect serum reproductive hormone levels in humans. In previous animal experiments, Maca was reported to show increased plasma levels of oestradiol for the single dose of 7.5 g/kg Maca powder in rats (Meissner et al., 2006a). Similarly, a high dose of Maca powder provided nutritional value: the total serum proteins and albumin were significantly superior in the mice fed 30% Maca (Canales et al., 2000). The changes of biomarkers in serum levels occur just in the high doses of Maca intake in

rodents. The present study showed that the LH-enhancing effect appeared for higher intakes of more than 15 g/kg of Maca powder. Traditionally, the natives in Junín still consume Maca meal two to three times per week and around 50 to 100 g per person per meal (Hermann and Bernet, 2009). Moreover, Valerio and Gonzales reported that most of the natives in the central Andes had used Maca in daily amount more than 100 g per day (Valerio and Gonzales, 2005). Although the daily intake of Maca in humans has changed along the times, Maca intake of high doses had been used in the Andean diet which the Spaniards found to attribute well-fed and tall adults in the high Andes (Sanchez Leon, 1996). Maca intake in the rats in the present study is consistent with the traditional intake in humans in the Andes. Therefore, high dose intake of Maca may be necessary for fertility in humans or rats in an environmental condition.

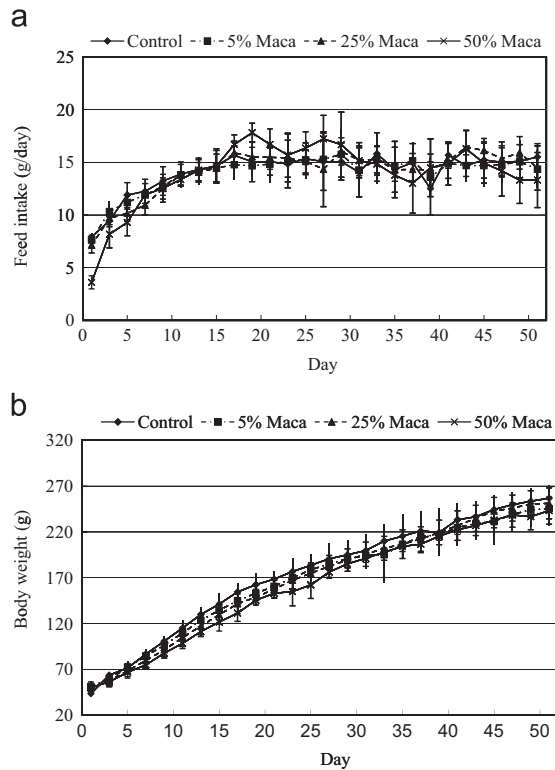


Fig. 1. Effects of Maca on body weight (A) and feed intake (B) in the rats. Food intake and body weight are represented in the control group ($n=20$ rats) and the groups received 5% ($n=10$ rats), 25% ($n=10$ rats), and 50% Maca feed ($n=20$ rats) after 7-week-old. Data are the means $\pm$ SD.

Table 2

Final body and absolute organ weights of 10-week-old rats fed with or without 50% Maca powder ($n=10$ /group).

Weight (g or mg)	Control group	50% Maca group
Body weight (g)	260.0 $\pm$ 20.7	237.6 $\pm$ 16.1
Pituitary (mg)	14.31 $\pm$ 2.60	15.71 $\pm$ 2.44
Hypothalamus (mg)	90.68 $\pm$ 19.21	88.58 $\pm$ 13.14
Right ovary (mg)	9.62 $\pm$ 1.23	11.26 $\pm$ 3.73
Left ovary (mg)	10.78 $\pm$ 1.48	11.60 $\pm$ 4.40
Uterus (mg)	34.38 $\pm$ 4.44	34.40 $\pm$ 3.41

All values represent mean $\pm$ SD.

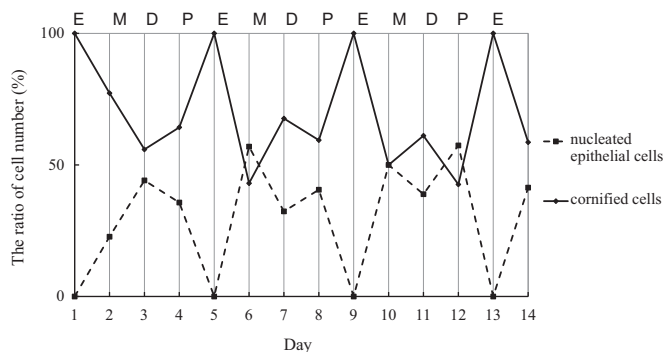


Fig. 2. An example of the 4-day oestrous cycle of the rats used. The vertical axis is the ratio of the number of nucleated epithelial cells to the number of cornified cells after 7 week-old. Each symbol is presented for the stages of pro-oestrus (P), oestrus (E), metoestrus (M), and dioestrus (D).

Table 3

Serum levels of pituitary hormones at 1800 $\pm$ 15 h of the pro-oestrus stage in 10-week-old rats fed with or without 50% Maca powder.

Pituitary hormones	Control group	50% Maca group
GH (pg/mL) ^a	1231.0 $\pm$ 725.5	1912.6 $\pm$ 1717.9
LH (ng/mL) ^a	4.9 $\pm$ 3.5	22.1 $\pm$ 10.7***
FSH (ng/mL) ^a	0.6 $\pm$ 1.0	9.45 $\pm$ 11.1**
PRL (ng/mL) ^a	18.8 $\pm$ 12.7	26.3 $\pm$ 6.9
TSH (ng/mL) ^a	2.4 $\pm$ 1.8	2.7 $\pm$ 3.7
ACTH (pg/mL) ^b	57.4 $\pm$ 25.9	119.4 $\pm$ 53.2*

All values represent mean $\pm$ SD.

^a $n=10$ /group.

^b $n=5$ /group.

* $P < 0.05$ vs. Control.

** $P < 0.01$ vs. Control.

*** $P < 0.001$ vs. Control.

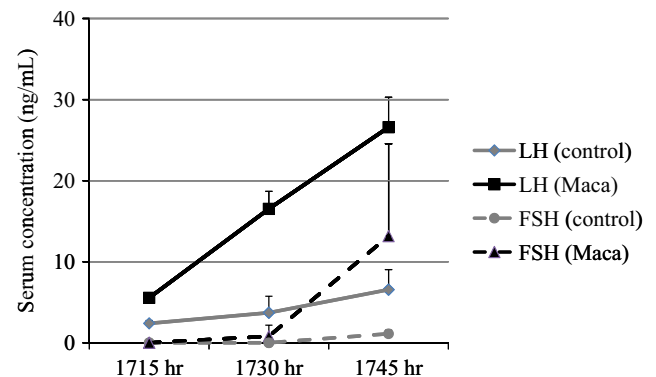


Fig. 3. The time course of elevated serum levels of LH ($n=10$) and FSH ($n=10$) in 10-week-old rats fed with or without 50% Maca powder.

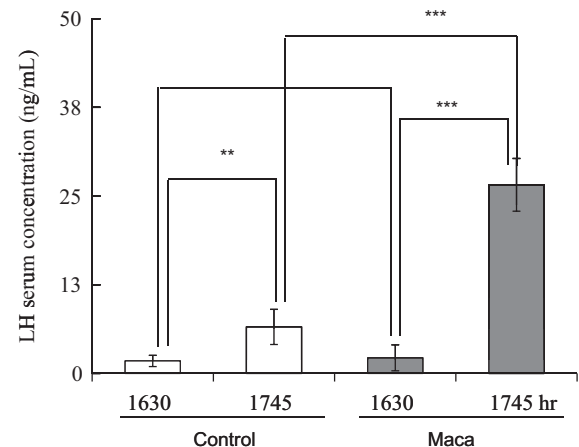


Fig. 4. The effect of Maca on the LH enhancement specified in the LH surge phase. The LH serum concentrations at 1630 h and 1745 h on the day of pro-oestrus are represented in the control group (1630 h, $n=4$, 1745 h, $n=3$) and the group received 50% Maca powder (1630 h, $n=3$, 1745 h, $n=4$) in 10-week-old rats. The values represent the mean $\pm$ SD. (** $P < 0.01$ and *** $P < 0.001$ vs. control group).

The present study demonstrated that the specific increases in LH serum levels among the pituitary hormones, the timing associated with the LH surge, and the subsequent FSH-releasing initiation exemplified the actions of Maca. These effects promote ovulation via the pituitary function of the HPG axis. Gonadotropin-releasing hormone (GnRH) regulates the mechanism of LH secretion. Environmental, nutritional, and physical conditions strongly influence the pro-oestrus LH surge. This information is integrated in the hypothalamus to signal LH secretion from the pituitary gland (Levine, 1997). Our findings indicate that the enhancement

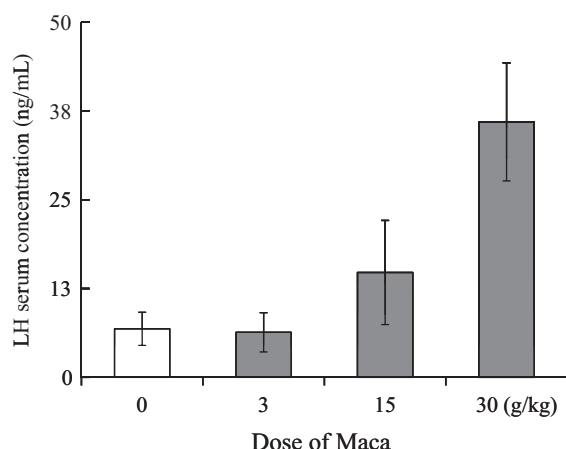


Fig. 5. Dose-response effect of Maca on the LH enhancement. The serum concentration of LH are presented in the control ($n=5$) and the Maca dose of 3 g/kg ($n=10$), 15 g/kg ($n=10$) and 30 g/kg ($n=5$) in 10-week-old rats. Maca doses are converted to g/kg using a body mass and dietary intake. Values represent the mean $\pm$ SD. (** $P < 0.01$ and *** $P < 0.001$ vs. control group).

of LH serum levels occurs during the normal menstrual cycle due to the pro-oestrus LH surge, and the menstrual cycle showed the same time course between the test and control groups (Fig. 3). The results of the present study might be useful for the study of the Maca response pathway by focusing on LH and its related proteins.

In conclusion, the traditional use of Maca for fertility was validated with respect to the enhancement of LH serum levels in female rats. The present study demonstrates that Maca (at the tested doses) enhances LH serum levels in the pituitary hormones of female rats during the LH surge and in a pharmacological, dose-dependent manner. These findings support the traditional use of Maca to enhance fertility and suggest a potential molecular mechanism responsible for its effects.

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