Published in final edited form as:
Plant Foods Hum Nutr. 2013 December ; 68(4): . doi:10.1007/s11130-013-0378-5.

Role of maca (*Lepidium meyenii*) consumption on serum interleukin-6 levels and health status in populations living in the Peruvian central Andes over 4000 m of altitude

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Abstract

Lepidium meyenii (Maca) is a plant that grows at over 4000 meters above sea level in the central Peruvian Andes. The hypocotyls of this plant are traditionally consumed for their nutritional and medicinal properties. The aim of this study was to determine the health status based on a health related quality of life (HRQL) questionnaire (SF-20) and serum levels of interleukin 6 (IL-6) in subjects that are maca consumers. For this, a cross-sectional study was designed to be performed in 50 subjects from Junin (4100 m): 27 subjects were maca consumers and 23 were non-consumers. The SF-20 survey is used to obtain a summary measure of health status. The stand up from a chair and sit down (SUCSD) test (to assess lower-extremity function), hemoglobin measurement, blood pressure, sexual hormone levels, serum IL-6 levels and the score of chronic mountain sickness (CMS) were evaluated. Testosterone/estradiol ratio ($P \ll 0.05$), IL-6 ($P < 0.05$) and CMS score were lower, whereas the health status score was higher, in maca consumers when compared to non-consumers ($P < 0.01$). A greater proportion of maca consumers successfully completed the SUCSD test compared to non-consumers ($P < 0.01$), showing a significant association with lower values of serum IL-6 ($P < 0.05$). In conclusion, consumption of maca was associated with low serum IL-6 levels and in turn with better health status scores in the SF-20 survey and low chronic mountain sickness scores.

Keywords

Lepidium meyenii consumption; IL-6; muscle strength; chronic mountain sickness; sex steroids; lower limb strength

Introduction

Maca (*Lepidium meyenii*) is a plant that grows at over 4000 meters in the central Peruvian Andes. The hypocotyls of this plant are traditionally consumed for their nutritional and medicinal properties [1]. Experimental scientific evidence showed that maca has nutritional,

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Conflict of interests: The authors have declared that no conflicts of interests exist.

energizing, and fertility-enhancing properties, and it acts on sexual dysfunctions, osteoporosis, benign prostatic hyperplasia, memory and learning, lipid and glucose metabolism and protects skin against ultraviolet radiation [2-5]. Clinical trials have shown efficacy of maca on sexual dysfunctions as well as increasing sperm count and motility without affecting serum hormone levels [6,12]. In the Peruvian population of Carhuamayo (4100 m), maca consumers aged 35-75 years old did not show a reduction of health status with age [13].

Maca constituents include fatty acids (palmitic, oleic, linoleic acids), sterols, aromatic glucosinolates and their derived isothiocyanates, and alkamides [1].

Life at high altitude (HA) is characterized by increased hemoglobin levels that in turn may produce oxidative stress [14]. This may account for a suggested earlier aging in highland populations compared to lowlanders [15]. In addition, excessive erythrocytosis is associated with a pathological condition named “chronic mountain sickness” (CMS) [16]. Serum IL-6 concentrations were increased during exposure to HA, but in values below the expected range in inflammatory diseases [17]. If IL-6 levels are also increased at HA populations, then this could affect health status.

Inflammation and oxidative damage are biological mechanisms for reducing health status. The inflammatory marker interleukin-6 (IL-6) is a robust predictor of the onset of negative health-related events [18]. In fact, high serum IL-6 levels have been associated with aging, obesity, increased incidence of cardiovascular disease [19,20], cognitive impairment [21], and more detrimental to survival among males than females [19-24]. Aging is associated with increased oxidative stress and circulatory changes that exacerbate inflammatory responses [25]. On the contrary, lower serum IL-6 levels were associated with higher values of physical fitness [26].

The hypothesis is that consumption at high altitudes may be associated with lower serum IL-6 values and these in turn higher scores in markers of health status. The present study was performed in Junin at 4100 m, another population in the central Peruvian Andes in which maca is consumed traditionally. The purpose of the study was to determine health status score, serum IL-6 levels and a marker of lower limb strength of maca consumers and comparing data with non-maca consumers.

Material and Methods

Subjects

This is a comparative study between a consuming maca group and another who do not consume maca, both residents at high altitudes. This study was approved by the Institutional Review Board (IRB) of the Universidad Peruana Cayetano Heredia. All volunteers gave written informed consent before the study. Fifty subjects (21 men and 29 women) aged 35-69 years and residents of the district of Junin at 4100 m, Peru were included in this study. Of these, 27 were maca consumers. Maca is prepared mainly at home and it is consumed as juice in 96% of the cases due its nutritional properties (100%), and by its medical properties (12%). The time consuming maca was 25.8±3.2 (mean±standard error of the mean) years (range 2-55 years). Fifty percent of the subjects studied consumed maca during the last 7 days, and 50% during the last month.

Subjects were randomly recruited at home. Subjects were allocated to the group of maca consumers or non-consumers, according to the results of a questionnaire. In addition, information regarding both the frequency and quantity of maca consumption was obtained, as well as the time that maca was last consumed.

A blood sample was drawn by venipuncture between 08.00 and 11.00 h. Blood samples were allowed to clot, and after centrifugation, serum was collected and stored in vials at −20°C until analysis. Height and weight was measured in the laboratory for each subject and their body mass index (BMI) was calculated as Kg/m^2.

Health Status Score

Health status was assessed using health related quality of life (HRQL) questionnaires. The survey used was adapted from the Short Form-36 Health Questionnaire Survey (SF-36), one of the most widely used questionnaires to evaluate quality of life [27]. In Peru, a shorter version of 20 questions (SF-20) was used and validated with populations both at sea level and at high altitude [13,28].

The original version (SF36), is a short-form health survey with 36 questions which measures 8 scale dimensions: Physical functioning scale, Role Physical scale, Bodily pain scale, General health, Vitality scale, Social functioning scale, Role-emotional scale and Mental health scale. After the validation, the Health Questionnaire included 7 dimensions, in which Social functioning scale was excluded [13]. The score from each question ranges from 1 to 3 or 4. Answers from each question were corrected to obtain a maximum value of 100%.

Lower limb strength

The stand up from a chair and sit down (SUCSD) test is a physical performance test used to assess lower-extremity function [29]. Lower-extremity function has been shown to predict subsequent development of disability because it reflects the effects of chronic disease, coexisting conditions, and overall physiologic decline. A 5 repetition test is a measure of strength.

Subjects were asked to rise from a chair, five times, as quickly as possible, with their arms folded and their hands on their shoulders. The chair had no arm rests. Subjects were instructed to stand up completely between repetitions. The results were qualified as “Yes”, if they were able to stand up 5 times without use the arms. Otherwise, the test result was recorded as “No”.

Hemoglobin (Hb) measurement

Hemoglobin concentration was measured on site with a HemoCue system (Anglholm, Sweden). Data were obtained in g/dl.

Blood pressure

At home and after an appropriate rest of 5 minutes, sitting systolic (SBP) and diastolic blood pressures (DBP) were measured in the left arm using an aneroid sphygmomanometer. Data were expressed as mm Hg.

Hormone levels

Serum testosterone (T) levels (ng/ml) and estradiol (E_2) levels (pg/ml) (DIAsource ImmunoAssays S.A, Nivelles, Belgium) were measured by radioimmunoassay using commercial kits. All assays required ^{125}I-labeled analyte. Minimum detectable concentration of serum T assay was 0.05 ng/ml, and 2 pg/ml for serum E2. The intra-assay coefficient of variation was 3.3% for T and 5.9% for E_2, and the inter-assay coefficient of variation was 4.8% for testosterone and 10% for estradiol.

Measurement of serum Interleukin-6 (IL-6)

Serum IL-6 levels were measured using the Human IL-6 ELISA set BD OptEIA Immunoassay kit (Becton Dickinson, San Diego, CA, USA). Samples were processed for ELISA determinations following the manufacturer's recommendations.

Chronic mountain sickness score (CMS score)

All participants completed a test for signs and symptoms of CMS. The test included 7 signs/symptoms: 1) breathlessness and/or palpitations; 2) sleep disturbance; 3) cyanosis, 4) dilation of veins, 5) paresthesia, 6) headaches, and 7) tinnitus. A value of 0 was assigned to negative answers and values from 1, 2 and 3 to positive answers (mild, moderate and severe, respectively) as stated by consensus [16]. For diagnosis of CMS a value of 3 was added if Hb value was ≥21 g/dl in men and >19.5 g/dl in women [16].

Statistical Analysis

Results were recorded in a database and analyzed using the statistical package STATA (version 10.0, Corporation, 702 University Drive East, College Station, TX, USA). Data are expressed as mean±standard error of the mean (SEM). The homogeneity of variances was determined with the Bartlett test. If homogenous, when more than two groups were compared, the analysis of variance test was used to determine differences among groups. If there were differences, the mean comparisons between each one of the groups were determined using the Scheffé test. In cases in which only two groups were compared, the Student t test was used to determine differences between means. The variables with no homogenous distribution were transformed to obtain a normal distribution. Data obtained as frequencies were analyzed using the chi square test or the Fisher exact test. Bivariate analyses were performed between age and health status score, and between age and serum IL-6 levels. If the regression was significant, age was incorporated in the multiple regression analysis. Multivariate regression analyses were assessed to determine the association of maca consumption and age with serum IL-6 levels, and to determine the association between, age, sex, IL-6 levels with health status score. Sex and maca consumption were defined as dichotomic variable. A value of $P<0.05$ was considered as statistically significant.

Results

Sex proportion and age were similar between groups of maca consumers and non-consumers ($P>0.05$). The analysis in Table 1 shows that systolic blood pressure, serum T levels, T/E_2 ratio, serum IL-6, and score for chronic mountain sickness were lower whereas, serum E_2 levels, and health score were higher in subjects who consumed maca.

A higher proportion of maca consumers (96.5%) successfully completed the SUCSD test compared to non-consumers (60.86%) ($P<0.01$). In subjects grouped according to serum IL-6 levels, the proportion of subjects with IL-6 levels >10 pg/ml that successfully completed the task was 50.9%, a value lower than that for subjects with serum IL-6 levels 1-10 pg/ml (81.48%) and serum IL-6 levels <1 pg/ml ($P<0.05$).

Subjects consumed maca in 41.68±8.49 days per year. Those consuming maca during the week of the study had serum IL-6 levels of 1.61±0.51 pg/ml, whereas those consuming maca the month before the study showed values of 2.98±0.82 pg/m ($P>0.05$). A significant difference was observed in the IL-6 levels of subjects that consumed maca within the week of the study compared with non-consumers (10.07±3.62 pg/ml) ($P<0.05$). Subjects with the lowest IL-6 levels (≤5 pg/ml) consume maca in greater quantities and for a longer time than those with IL-6 levels >10 pg/ml. None of the subjects with IL-6 >10 pg/ml consumed maca. While IL-6 levels were reduced, the proportion of maca consumers was increased

(Table 2). In the multiple regression analysis, maca consumption was inversely associated with serum IL-6 after controlling for chronological age (Table 3). Health status scores were inversely related with age and serum IL-6 levels were higher in men (Table 4).

Discussion

In this population-based study, significant associations between maca consumption, low serum IL-6 levels and high health status were observed. Previously, it was demonstrated that maca consumer subjects in Carhuamayo at 4100 m have better health scores than non-maca consumers [13]. In Junin (4100 m), located close to Carhuamayo, maca consumers also have better health scores. In addition, the levels of serum IL-6 were lower in subjects who consumed maca.

The low levels of serum IL-6 may explain why the group of maca consumers showed lower systolic blood pressure, lower CMS score and higher health score in the survey. Higher IL-6 production plays an important role in the development of several age-related conditions including elevated systolic blood pressure [30]. In our study, the group with higher IL-6 levels had higher systolic blood pressure. Plants with anti-atherogenic potential also produce low IL-6 levels [31]. It has been suggested that maca also has an anti-atherogenic effect [5]. IL6 levels may be maintained without changes in an individual after assessment during three consecutive mornings, but there is a significant inter-variability [32]. For this reason, in future studies serial measurements should be performed. It is considered that until plasma IL-6 differences exceed 0.32 pg/ml, such values should be considered normal fluctuations between trials [32]. In our study, the difference in IL-6 between maca consumers and non-consumers was 7.84 pg/ml.

IL-6 was elevated under acute [17] or chronic [33,34] exposure to hypoxia conditions. If hypoxia increases IL-6, in native populations living at high altitudes, then the lower serum IL-6 levels observed in subjects in Junin, who are maca consumers, may suggest that maca could be acting to inhibit the high altitude-induced increase in IL-6. However, a prospective study is required to evaluate this hypothesis.

In the SUCSD test to evaluate lower limb strength, it was observed that a favorable outcome was more likely in subjects who consume maca and in those with lower IL-6 levels. This is in line with data from other authors [26] who found that low serum IL-6 levels are associated with high 6-minute walking performance.

Recent studies in normal populations showed that serum IL-6 levels were associated with serum testosterone and estradiol levels [35].

From these data, it is suggested that T influences an increase in IL-6 whereas E_2 seems to show opposed effects [36-38]. These data suggest that higher T/E_2 levels are associated with high IL-6 levels. In our study, highland subjects who do not consume maca have higher serum T/E_2 ratio associated with higher serum IL-6 levels. In addition, subjects with higher T/E_2 ratio have also higher score of CMS. Higher T levels were associated with higher CMS score [39]. The finding that maca consumption was associated with low serum T/E_2 ratio and low CMS score suggest that this plant could be an alternative treatment option for this disease.

This is a cross-sectional based study. For such reason, it is difficult to demonstrate a cause-effect relationship between maca consumption and serum IL-6 levels. A prospective study is required.

Conclusions

Serum IL-6 levels were reduced in the maca consuming population and this was associated with low systolic blood pressure, high health score, and a lower score of CMS. The high IL-6 levels in subjects at high altitude seem to be associated with high serum T/E_2 levels and this elevated ratio could be reduced by consumption of maca.

Acknowledgments

We thank the staff of the Laboratory of Endocrinology & Reproduction at the Universidad Peruana Cayetano Heredia and from Health Centers in Junin.

Funding: This study was supported by a NIH Research Grant # 5-D43TW005746-04 funded by the Fogarty International Center, National Institutes on Environmental Health Services, National Institute for Occupational Safety and Health, and the Agency for Toxic Substances and Disease Registry.

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Table 1

Variables associated with consumption of maca hypocotyls in subjects living in Junin at 4100 m altitude in Peru.

Variable	Maca Consumers (n=27)	Non consumers (n=23)	maca P
Males/Females	0.69	0.76	>0.05
Age (years)	46.1±1.58 (35-60)	50.0±2.17 (35-69)	>0.05
Systolic blood pressure (mm Hg)	113±2.45 (90-140)	120±1.65 (100-140)	<0.05
Diastolic blood pressure	72.8±2.09 (60-100)	78.2±2.64 (50-90)	>0.05
Body mass index (Kg/m^2)	25.7±0.79 (19.4-33.9)	27.6±0.73 (22.6-36.3)	>0.05
Hemoglobin (g/dl)	17.5±0.37 (12.6-20.3)	18.0±0.38 (14.9-21.5)	>0.05
Testosterone (ng/ml)	3.56±0.72 (0.52-12.71)	6.98±0.95 (0.24-13.21)	<0.05
Estradiol (pg/ml)	82.4±8.71 (10.0-129)	40.0±8.68 (12.4-110)	<0.01
Testosterone/Estradiol *1000[a]	189±67.1 (5.4-886)	299±67.8 (15.9-829)	<0.05
IL-6 pg/ml	2.23±0.46 (0-9.5)	10.07±3.62 (0-64)	<0.05
Health score/10[a]	165±2.43 (135-190)	134±8.23 (67-193)	<0.01
CMS score	2.38±0.36 (0-7)	4.47±0.67 (0-11)	<0.01

[a]Data were transformed to logarithm for analysis. Sex proportion was assessed with chi square test. Data are mean±standard error of the mean. P=Probability. IL-6= Interleukin 6. CMS score: score of signs and symptoms of chronic mountain sickness.

Table 2

Characteristics of maca consumption in subjects from Junin (4100 m) in relation with levels of serum interleukin 6 (IL-6)

Interleukin 6 (pg/ml)	Time consuming maca (years)	Days consuming maca/year	Hypocotyls/day (gram)	% subjects consuming maca[c]
0-1	17.8±4.48*	41.9±4.48[a]	15.9±3.08*	80
>1-5	18.7±4.77*	23.1±7.74	10.8±2.71*	63
>5-10	10.0±5.00**	9.50±6.37	8.13±4.22	38
>10	0.00±0.00	0.00±0.00	0.00±0.00	0

Data are mean ± standard error of the mean.

* P<0.01;

** P<0.05 with respect to IL-6>10 pg/ml.

[a] P<0.01 with respect to the group with IL-6 >5-10 pg/ml.

[c] P<0.01, chi square test.

Table 3

Multiple regression analysis to test the probability that serum interleukin 6 (IL6) level is associated with maca consumption and age.

Serum IL-6	Coefficient of Regression	Standard Error	T	P>|t|	[95% Conf. Interval]
maca consumer	−5.17	1.50	−3.45	0.001	−8.19 −2.15
Age	−.024	.069	−0.35	0.730	−.162 .114
Constant	13.7	5.00	2.74	0.009	3.63 23.8

Table 4

Multiple regression analysis to test the probability that health status score is associated with age, serum interleukin 6 (IL-6) levels, and sex.

Health status score	Coefficient of Regression	Standard Error	T	P>|t|	[95% Conf. Interval]
Age (years)	−18.8	2.76	−6.82	0.000	−24.4 −13.2
Serum IL-6	−16.5	5.73	−2.88	0.006	−28.0 −4.95
Sex	240	60.1	3.99	0.000	119 361
Constant	2187	153	14.30	0.000	1878 2495

Sex: 1: Female; 2: Male