Acute and Chronic Dosing of *Lepidium meyenii* (Maca) on Male Rat Sexual Behavior

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DOI: 10.1111/j.1743-6109.2007.00437.x

ABSTRACT

Introduction. The use of natural remedies for the treatment of sexual disorders is under current investigation. For generations people of the rural community in Peru have used *Lepidium meyenii* Walpers (Maca), because of their belief that it improves fertility and sexual desire.

Aim. To determine the acute and chronic effects of Maca on male sexual behavior and to examine chronic administration of Maca on anxiety.

Main Outcome Measures. Ejaculatory and mounting behavior and postejaculatory interval. Anxiety tests using an elevated plus maze, locomotion, and social interaction with another male.

Methods. Maca (25 and 100 mg/kg) was orally administered to male rats for 30 days. Male sexual behavior was monitored after acute, 7 and 21 days of treatment. Anxiety behavior and locomotion were measured at 28–29 days using the elevated plus maze and social interaction tests.

Results. Maca treatment did not produce large changes in male sexual behavior. However, an increase in ejaculation latency and postejaculatory interval was observed after both acute and 7 days of treatment. After 21 days of treatment Maca had no effect on sexual behavior. Chronic administration of Maca did not increase locomotion or anxiety.

Conclusion. Acute and short-term administration of Maca produced a small effect of rat male sexual behavior and long-term administration did not increase anxiety. **Lentz A, Gravitt K, Carson CC, and Marson L. Acute and chronic dosing of *Lepidium meyenii* (Maca) on male rat sexual behavior. J Sex Med 2007;4:332–340.**

Key Words. Ejaculation; Elevated Plus Maze; Social Interaction; Postejaculatory Interval; Herbal Remedies

Introduction

Sexual health and function are important to all species. In humans, disorders such as erectile dysfunction and female sexual dysfunction are becoming increasingly more important as a result of associated sexual side-effects with various diseases, increased awareness, availability of treatment options, and the aging population [1–6]. Men and women of all ages seek guidance in an effort to improve their relationships, experience satisfying sexual lives, as well as to improve fertility. Successful treatment of reproductive disorders has been demonstrated to improve overall quality of life, and relieve symptoms of depression [2,4,7,8].

A number of naturally grown plants have been used as traditional treatments, one of these plants, *Lepidium meyenii* Walpers (Maca), a crop that is found in a restricted area of Peru, has a long history and traditional use and has been reported to increase fertility and improve sexual function [9–12]. Self-reported levels of sexual desire were significantly greater in men after chronic Maca treatment compared with the placebo group and the Maca group showed lower Hamilton rating scores for depression [13]. An increase in semen volume and total sperm count was also reported after chronic Maca treatment [10]. However, 2–12 weeks of treatment with Maca did not alter steroid hormone levels [11]. Research studies in rodents have also suggested that Maca improves sexual function [14–17]. In mice chronic administration of Maca was shown to increase the total number of intromissions observed over a 3-hour period [16]. In rats, a reduction in the latency to

mounting behavior was observed in sexually experienced rats after both acute and chronic Maca treatment [14]. Maca treatment also increased weight of the testes, and epididymus and changed the rate of spermatogenesis [17–20].

One difficulty in assessing the use of herbal preparations is the lack of standardization of these products. As they are generally categorized as food additives by the Food and Drug Administration there is little or no oversight of their production and distribution in the United States. The absence of regulatory control is likely to lead to marked differences in purity and content among herbal products [21]. Although there is much speculation about which specific compounds in Maca are responsible for its aphrodisiac and fertility-enhancing actions, there is no clear conclusive evidence regarding this subject. Some studies of Maca seem to be related to its property as a nutrient, for male fertility and for energy, while other studies suggest that secondary metabolites found in Maca extracts are important constituents responsible for its physiological effects [12,22–24].

Aim

This study was designed to further investigate the acute and chronic effects of Maca on male sexual behavior and to determine which sexual parameters are influenced. In addition, behavior in an elevated plus maze, social interaction, and locomotion were examined to examine the effect of long-term dosing of Maca on anxiety.

Methods

Animals

Studies were performed on male and female Sprague–Dawley rats (250–350 g, Charles River Laboratories, Wilmington, MA, USA) housed in the same facility. Female rats were ovariectomized by Charles River Laboratories prior to arrival. Animals were given ~2 weeks to adapt to the light–dark cycle, with lights off at 08:00; on at 20:00 hours. Male rats were housed three per cage and sexually experienced on two to three prior occasions by pairing with a receptive female, only males that consistently ejaculated during preliminary trials were selected for the studies. All procedures were in accordance with federal and institutional regulations on the care and use of animals for scientific purposes.

Treatments

Sexually experienced male rats were randomly assigned to one of the treatment groups. Groups of rats (N = 11 per group) received distilled water, 25 or 100 mg/kg of the aqueous solution of Maca (Natura-max S.A.C., 100% natural) via oral gavage daily (1 mL/kg) for 30 days. Dosing took place between 07:00 and 08:00 hours. On day 1 (acute administration) male rats received the Maca or distilled water 25–30 minutes before the onset of sexual behavior. On day 7 and 21 male sexual behavior was examined 4–7 hours after oral dosing. Females were brought into estrus by sequential treatment with estradiol 3-benzoate (20 μg/kg subcutaneously in sesame oil; Sigma, St. Louis, MO, USA) 48 hours prior to testing, followed by progesterone (2 mg/kg s.c. in sesame oil; Sigma) at least 3 hours before testing.

Sexual Behavior

Behavior was recorded during the early phase of the dark cycle by video under red light. Later a trained, validated observer, blinded to the treatment group, scored the sexual behavior. Male rats were placed into a large (20 × 14 inches) clean cage for 15 minutes before the female was introduced and sexual behavior was recorded for 40 minutes. The number of attempted mounts, mounts, intromissions, and ejaculations were recorded. In addition, the intromission latency (time from presentation of the female to the first intromission); ejaculation latency (time from the first intromission to ejaculation); postejaculatory interval (time from an ejaculation to the first intromission); copulatory efficiency (the number of intromissions divided by the number of mounts plus intromissions); intercopulatory interval (latency to ejaculation divided by the number of intromissions) were calculated. Data are presented for the first three ejaculatory series recorded in each session.

Elevated Plus Maze

On day 28 of daily dosing, animals were tested in an elevated plus maze [25,26] that consisted of two opposite open arms and two opposite enclosed arms (with 40-cm-high walls), made of black Perspex. The arms were connected by a central 10 × 10 cm square, and the maze formed a "plus" shape that was elevated 50 cm off the ground. The behavior was examined under dim light with a video camera mounted vertically over the maze that was recorded and scored "off line" by a person blinded to the treatment groups. Animals were initially placed in the center of the apparatus and their behavior recorded for 5 minutes. The latency to enter an arm, number of entries, and amount of time spent in the open and closed arms (defined by

all four paws in arm) or in the center (default position) and the number of rears, head dips, stretch attends (body and head stretched out on all four paws) were recorded for each animal.

Social Interaction and Locomotion

Animals were tested in the social interaction arena [25,27,28] on day 29. The arena consisted of an open field (60 cm × 60 cm) surrounded by four walls that was divided into 16 equal squares. Two animals from the same treatment group, but from different cages, were placed on opposite sides of the open field and allowed to move freely and interact for 5 minutes, under low light conditions. The behavior was recorded by a video camera mounted vertically over the arena and scored "off line" by a person blinded to the treatment groups. The total number of lines crossed and the amount of time the animals spent in the center squares vs. the side squares were summed and recorded for each pair [27] to indicate locomotion. Similarly, we counted the number of follows, self-grooms, grooming partner, mounts, genital sniffs, rears, and general sniffs, as well as aggressive or defensive behavior and summed the scores of each pair; these measure indicate anxiety and social behavior.

Statistical Analysis

Statistical analyses were performed using one-way ANOVA (followed by Dunnett's post hoc test only when an overall significance was determined). The unpaired *t*-test was also performed to compare the control group with each dose of Maca. A value of $P < 0.05$ was considered statistically significant.

Results

Male Sexual Behavior

Acute Administration

Acute administration of Maca did not significantly alter the number of intromissions or mounts observed in each ejaculatory series (Figure 1). There was no significant difference in the number of ejaculations each group experienced during the testing period (control—3.3 ± 0.2; 25 mg/kg—3.6 ± 0.2; 100 mg/kg—3.9 ± 0.2 [mean ± SE]). However, the Maca groups tended to have more variability in the number of mounts compared with the controls and the average number of mounts plus intromissions and the number of ejaculations tended to be higher after Maca (Table 1, see above). The mean latency to the first and second ejaculation was longer after treatment with Maca and the postejaculatory interval appeared to increase over time in the Maca-treated groups (Figure 1). There were no differences in intromission latency between the groups (mean range 23–29 seconds) suggesting that the delay in ejaculation was not due to delayed initiation of mounting behavior. There were no major differences in the overall copulatory efficiency or intercopulatory interval (Table 1).

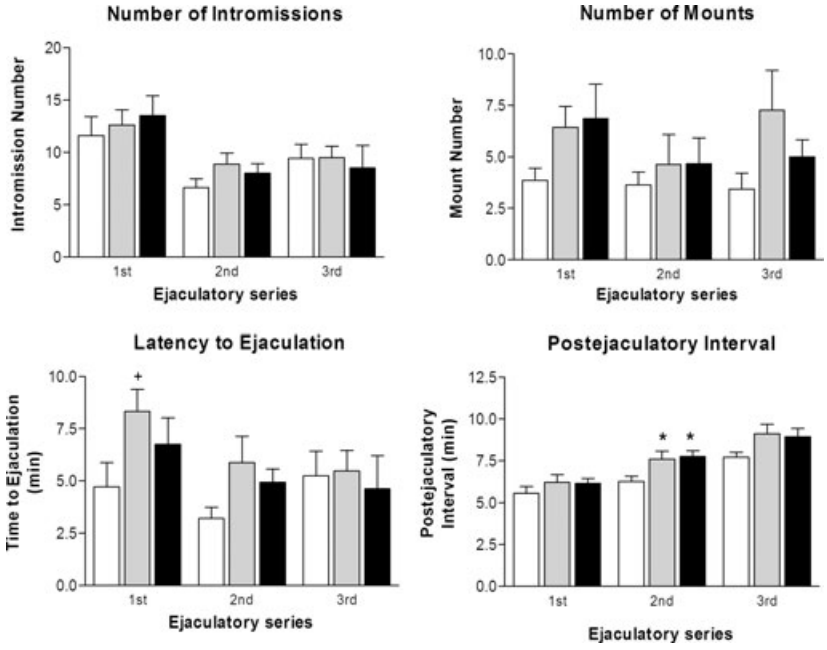

Figure 1 Effects of acute administration of Maca on male sexual behavior. Data (mean ± SE) are shown for the first three ejaculatory series. Water or Maca was administered 10 minutes before the onset of sexual behavior. Control (water) group—open bars; 25 mg/kg Maca—gray bars; 100 mg/kg Maca—black bars. Number of rats per group = 6–9. The asterisk (*) indicates a significant difference from controls determined by Dunnett's post hoc test (ANOVA, overall effect; $P = 0.025$ postejaculatory interval). The cross (+) indicates a difference from controls (unpaired *t*-test $P = 0.037$).

Table 1 Effects of acute administration of Maca on male sexual behavior

Ejaculatory series	Treatment	Copulatory efficiency	Intercopulatory interval	Mounts plus intromissions
First	Control	0.74 ± 0.03	0.41 ± 0.10	15 ± 2.1
	25 mg/kg	0.66 ± 0.05	0.68 ± 0.06*	19 ± 1.8
	100 mg/kg	0.69 ± 0.07	0.51 ± 0.07	20 ± 2.9
Second	Control	0.66 ± 0.05	0.50 ± 0.06	10 ± 1.1
	25 mg/kg	0.71 ± 0.07	0.64 ± 0.05	14 ± 2.2
	100 mg/kg	0.66 ± 0.07	0.63 ± 0.06	13 ± 1.2
Third	Control	0.75 ± 0.05	0.46 ± 0.05	13 ± 1.9
	25 mg/kg	0.62 ± 0.06	0.56 ± 0.07	17 ± 2.6
	100 mg/kg	0.62 ± 0.03	0.50 ± 0.04	14 ± 3.6

Data (mean ± SE) are shown for the first three ejaculatory series. Water or Maca was administered 10 minutes before the onset of sexual behavior. N = 6–9.
*A difference from control group (unpaired *t*-test $P = 0.0370$).

Seven Days of Treatment

After 7 days of treatment with Maca there was a tendency to an increase in the number of intromissions and mounts (Figure 2, Table 2). There was no significant effect on the number of ejaculations each group experienced during the testing period (control—3.9 ± 0.3; 25 mg/kg—3.4 ± 0.2; 100 mg/kg—3.7 ± 0.2 [mean ± SE]). As found after the acute dosing, 7 days of treatment with Maca resulted in a delay to the first ejaculation (Figure 2); this effect dissipated in subsequent ejaculatory series. Even though the time to the first ejaculation was increased with Maca the latency to the first intromission tended to be shorter in the Maca groups (control, 32 ± 11; 25 mg/kg, 24 ± 8; 100 mg/kg, 18 ± 7; [mean ± SE seconds]). Therefore, the delay in ejaculation was not due to a delay in the initiation of mounting behavior. The postejaculatory interval increased significantly with administration of Maca (Figure 2). There were no major differences in the copulatory efficiency or intercopulatory interval (Table 2).

Twenty-One Days of Treatment

By 21 days of daily dosing with Maca no significant differences in male sexual behavior were seen between the groups in any parameters examined (Figure 3). In addition, the number of ejaculations each group experienced was similar (control—4.1 ± 0.4; 25 mg/kg—3.8 ± 0.3: 100 mg/kg—4.0 ± 0.0 [mean ± SE]).

Elevated Plus Maze

Maca (100 mg/kg) treatment significantly increased the time rats spent with all four paws in

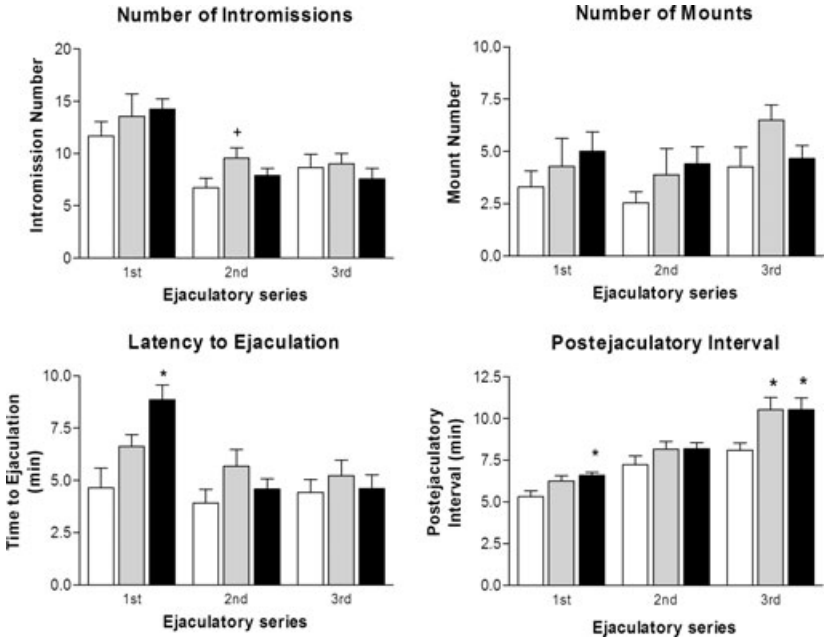

Figure 2 Effect of 7 days of administration of Maca on male sexual behavior. Water or Maca was administered once daily for 7 days. Sexual behavior was tested 4–7 hours after dosing on day 7. Data (mean ± SE) are shown for the first three ejaculatory series. Control group—open bars; 25 mg/kg Maca—gray bars; 100 mg/kg Maca—black bars. Number of rats per group = 8–11. The asterisk (*) indicates a significant difference from controls determined by Dunnetts' post hoc test (overall significance using ANOVA: first ejaculatory series—$P = 0.017$ latency to ejaculation; $P = 0.011$ postejaculatory interval. Third ejaculatory series—$P = 0.003$ postejaculatory interval). The cross (+) indicates a difference from controls (unpaired *t*-test $P = 0.0493$).

Table 2 Effects of 7 days of administration of Maca on male sexual behavior

Ejaculatory series	Treatment	Copulatory efficiency	Intercopulatory interval	Mounts plus intromissions
First	Control	0.74 ± 0.06	0.42 ± 0.07	15 ± 1.3
	25 mg/kg	0.76 ± 0.05	0.53 ± 0.06	18 ± 3.0
	100 mg/kg	0.80 ± 0.08	0.61 ± 0.06	19 ± 1.5
Second	Control	0.74 ± 0.05	0.61 ± 0.07	9 ± 1.2
	25 mg/kg	0.74 ± 0.06	0.59 ± 0.05	13 ± 1.4*
	100 mg/kg	0.65 ± 0.04	0.58 ± 0.03	12 ± 1.3
Third	Control	0.68 ± 0.07	0.63 ± 0.13	13 ± 1.9
	25 mg/kg	0.58 ± 0.02	0.59 ± 0.07	16 ± 1.6
	100 mg/kg	0.61 ± 0.05	0.63 ± 0.06	12 ± 1.2

Data (mean ± SE) are shown for the first three ejaculatory series. Water or Maca was administered daily for 7 days and sexual behavior was examined 4–7 hours after dosing on day 7. N = 8–11.
*A difference from control group (unpaired *t*-test $P = 0.0378$).

Table 3 Effects of 28 days of administration of Maca on elevated plus maze behavior

Treatment	Time spent in center	Ratio of open/(open + closed) arm entries	Percent time in open/(open + closed) arm	Latency to enter arm (second)
Control	120 ± 12	0.19 ± 0.04	22 ± 5	7.5 ± 2.4
Maca 25 mg/kg	129 ± 10	0.19 ± 0.03	24 ± 5	10.8 ± 3.0
Maca 100 mg/kg	159 ± 9*	0.14 ± 0.06	14 ± 6	3.9 ± 0.8

Water or Maca was administered daily for 28 days and behavior was examined 4–7 hours after dosing on day 28. Values are mean ± SE. N = 9–10.
*A significant difference (ANOVA $P = 0.0338$).

the center, which was interesting as this Maca group also had the shortest latency to move out of the center, which was the initial placement (Table 3). These data suggest that this group may have been less anxious. There were no significant differences between the three groups in the time spent in the open vs. the closed arm or which arm rats favored entering (Table 3). No differences were found in the number of other behaviors recorded, such as rears, head dips, or feces produced.

Social Interaction and Locomotion

The low-dose Maca group crossed fewer lines compared with the control group (Table 4),

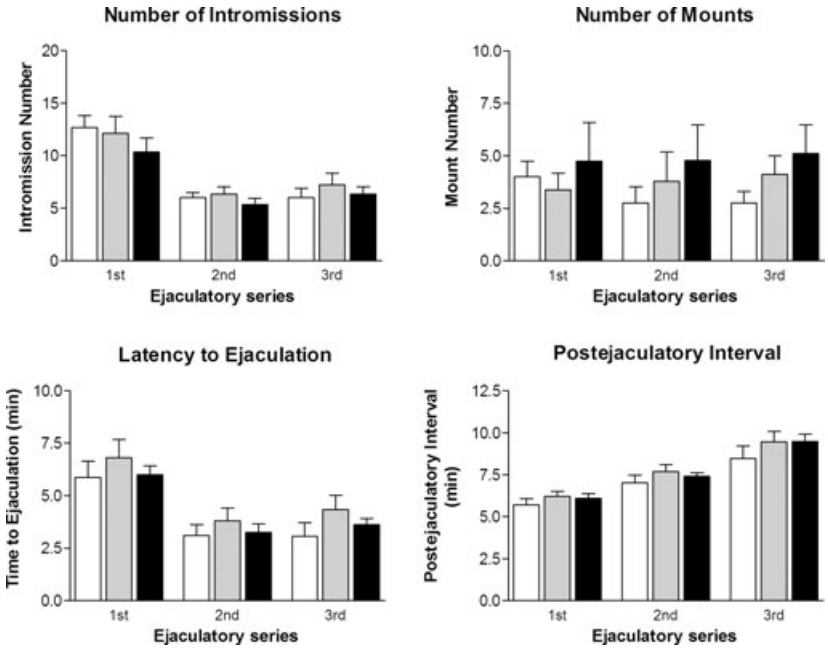

Figure 3 Effects of 21 days of administration of Maca on male sexual behavior. Water or Maca was administered once daily for 21 days. Sexual behavior was tested 4–7 hours after dosing on day 21. Data (mean ± SE) are shown for the first three ejaculatory series. Control group—open bars; 25 mg/kg Maca—gray bars; 100 mg/kg Maca—black bars. Number of rats per group = 8–11.

Table 4 Effects of 29 days of administration of Maca on locomotion and social interaction behavior

Treatment	Number of lines crossed	Percent time spent in center/total	Number of self-grooms	Number of social grooms	Number of follows	Number of genital sniffs
Control	273 ± 10	12 ± 1	3.6 ± 0.5	1.2 ± 0.4	11 ± 2	14 ± 3
Maca 25 mg/kg	225 ± 7*	12 ± 2	2.0 ± 0.7	0.5 ± 0.3	7 ± 1	15 ± 2
Maca 100 mg/kg	253 ± 7	15 ± 2	3.0 ± 1.2	0.2 ± 0.2†	9 ± 1	18 ± 3

Water or Maca was administered daily for 28 days and behavior was examined 4–7 hours after dosing on day 28. Values are mean ± SE. N = 9–10.
*A significant difference from control group (ANOVA $P = 0.007$).
†A difference from control group (unpaired *t*-test $P = 0.0460$).

suggesting that this group was less active than the other groups. The amount of time spent in the center vs. the periphery of the open field was comparable between all groups. No major differences in any behaviors recorded were seen between the control and Maca-treated groups, although there was a trend in the Maca groups to groom their partners less than the controls (Table 4).

Discussion

The present study shows that acute and daily administration of Maca in sexually experienced Sprague–Dawley male rats did not produce a large effect on sexual performance, which may be expected from administration of a natural product. However, an increase in the latency to the first ejaculation was observed after acute and 7 days of administration of Maca, without a delay in the initiation of mounting behavior. In addition, a significant effect was found on postejaculatory interval. By 21 days of treatment no differences in sexual behavior were found between the control and Maca groups. Chronic administration of Maca did not increase anxiety in male rats. Chronic administration of Maca (25 mg/kg) decreased locomotion.

Previous studies examining the effect of Maca on sexual behavior suggested that both acute and chronic administration of Maca in either sexually naive or experienced male rodents had some facilitatory effect on sexual behavior [14–16]. An increase in the number of intromissions was reported in mice over a 3-hour recording period after 22 days of treatment with Maca. In rats, a decrease in intromission latency after both acute and chronic administration of Maca, with the hexanic extract demonstrating the greatest change in mounting behavior, was observed [15]. However, an increase in locomotor activity was also observed after 12 days of administration of Maca that may have contributed to reduction in latency to mounting behavior [14]. Administration of Maca has also been shown to decrease the latency to electrically evoked penile erections in rats with their testes removed, with high doses (180–1,800 mg/kg/day) of Maca [16]. Other studies in rodents have demonstrated that Maca treatment enhances spermatogenesis [17,18], which may be related to the enhancement of fertility reported in humans [10–12,29]. In the present study the latency to ejaculation increased with Maca. It is interesting to note that female rats normally pace the sexual contacts by the male and under these circumstances it takes longer for the males to ejaculate [30,31]. These reports and the present study all agree that Maca has some effect on sexual behavior. The differences between the present study and previous studies may be related to the source and dose of Maca extract tested or different experimental protocols and analysis that may include the level of prior sexual experience.

The disappearance of the effects on sexual parameters by 21 days of daily dosing of Maca in the present study suggests tolerance may have developed. In addition, the repeated successive weekly sexual experience may have led to an attenuation of the effect of the drug on sexual behavior. However, further studies need to be performed in separate groups of sexually naive and experienced animals dosed for varying time frames in order to investigate these possibilities.

Social behaviors indicative of anxious animals include following, sniffing, and grooming another animal and increased time in closed arms of the elevated plus maze or reluctance to enter open arms [25–28,32]. In the present study the low-dose Maca (25 mg/kg) showed less locomotor activity in the social interaction arena compared with the controls. No clear evidence for increased or reduced anxiety using the elevated plus maze and the social interaction arena was observed. A reduction in anxiety related to administration of Maca was suggested in a recent study that used higher doses (1 g/kg) of Maca varieties and used the forced swim test in ovariectomized mice [32]. This study concluded that Maca showed an antidepressant effect on the mice since a reduction in the

immobility times was observed. In men it remains unclear if Maca decreases anxiety; studies have shown an increased sexual desire with Maca treatment without any adverse affect on mood [11]. Further clarification of Maca's effect on anxiety is required by examining animals in various anxiety tests that have not been subjected to prior successive sexual behavior.

At the present time it is difficult to ascertain if the effect of Maca on sexual performance is due to a direct effect of an active product of Maca or to an indirect effect. Sexual desire and performance may be affected by several factors including general good health, testosterone levels, stress, and anxiety [4,5,33–35]. Adequate clinical evidence to support natural agents for the management of male sexual dysfunction is minimal and the Maca extract appears to have a modest and differential effect on sexual behavior in male rats. However, chronic Maca treatment did not significantly increase anxiety. Further studies with standardized Maca ingredients are required to more clearly confirm the effect of Maca on sexual behavior.

Conclusion

The present study demonstrated that acute and daily administration of Maca in sexually experienced male rats produced a small change in ejaculation latency and postejaculatory interval and these changes disappeared with chronic treatment. Chronic administration of Maca did not increase anxiety and had some effect on locomotor activity.

Acknowledgments

This work was supported in part by a short-term research training grant from National Institute of Diabetes and Digestive and Kidney Disease to Aaron Lentz and National Institute of Health grant NS39166 to Lesley Marson.

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Conflict of Interest: None declared.

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Commentary on Lentz A, Gravitt K, Carson CC, Marson L. Acute and Chronic Dosing of *Lepidium meyenii* (Maca) on Male Rat Sexual Behavior

This last decade an increasing number of scientific publications investigated the effects of medicinal plants on sexual behavior in animals. In the present study authors reported after acute and 7 days, but not 21 days of treatment with *Lepidium meyenii* Walpers (Maca) increased ejaculation latency and postejaculatory interval in rats, without delaying initiation of intromission or modifying copulatory efficiency. Twenty-eight days of treatment did not appear to produce anxiogenic effects, but the lowest dose seemed to slightly decrease locomotor activity after 29 days of treatment. The acute or 7 days of treatment effects were not investigated on anxiety-related parameters or locomotor activity. Attention should be paid to the effects of *Lepidium meyenii* Walpers (Maca) on sexual motivation, mood, or locomotion in parallel to sexual behavior testing.

What remains always difficult with natural compounds is the understanding of the underlying mechanisms of action. Which specific substances(s) in Maca may be responsible for its effects on sexual behavior? Are these effects exerted at the central or peripheral level? Which may be the possible side-effects of such herbal remedies? These questions are to be answered. Overall this study provides encouraging results concerning the effects of this herbal product on male sexual behavior in terms of its ability to delay ejaculation. As appropriately mentioned by

the authors, additional basic research should be performed, taking into account the previous pharmacological, physiological, and behavioral studies and using a standardized form of the product, to reinforce these preliminary positive outcomes. Currently there is still no approved compound for the treatment of premature ejaculation. Accordingly this study contributes to widen the field of research and knowledge concerning the effects of compounds, which may delay ejaculation and improve sexual life in men complaining of premature ejaculation.

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