Author’s response to reviews

Title: Effect of three different cultivars of Lepidium meyenii (Maca) on learning and depression in ovariectomized mice

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Author’s response to reviews: see over
Lima, May 19th 2006

Editorial Board, BMC Complementary and Alternative Medicine

I declare in this letter that the study titled: “Effect of three different cultivars of Lepidium meyenii (Maca) on learning and depression in ovariectomized mice” was conducted in compliance with “Guide of the care and use of laboratory animals” (National Research Council, 1996). Also, the Institutional Review Board of the Scientific Research Office from the Universidad Peruana Cayetano Heredia approved the study.

In this study we demonstrated that different ecotypes of Maca present different biological effects with respect to learning and depression. People in the Central Andes of Peru use Maca to treat the menopause symptoms, including cognitive function and depression and this study pretend to be the first that confirm this effect. We consider that this finding has a great importance for ethnopharmacology because the most frequent ecotype of Maca found in Carhuamayo, Junin, Peru is the Yellow Maca and also it is the most commercially preferred and the fact, for example, that Yellow Maca does not present effects on learning may cause a decline in the consumption of all existing ecotypes (13 ecotypes of Maca ranging from White to Black have been described). Here we found that Black Maca was the ecotype that presented beneficial effects on latent learning; meanwhile, all varieties of Maca presented antidepressant activity. These effects will enhance the commercial possibilities of these products and for their producers.

All comments made by the reviewers had been revised and modifications were made in the new version of the manuscript according to reviewers’ comments. At the end of this letter you can find the answer to each comment made by the reviewers. The revised manuscript conform to all of the points of the manuscript formatting checklist.

Finally, all authors revised the manuscript and we are agreed to submit the manuscript to the BMC Complementary and Alternative Medicine. The manuscript follows the format required to submit to your journal. Also, The authors declare that they have no competing interests.

Best regards,
ANSWER TO REVIEWER 1
Reviewer’s report
Effect of three different cultivars of Lepidium meyenii (Maca) on learning Title: and depression in ovariectomized mice
Version: 3 Date: 30 April 2006
Reviewer: Arrigo F.G. F Cicero
Reviewer’s report:

General

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

ANSWER: These have been corrected in the revised version
â€¢ Please, check the reference number: the 11. is not reported in the text.
ANSWER: Ref. 11 was reported in page 3 and page 11.

â€¢ Because of the relatively low number of tested animals, a box-plot graph could be more appropriated and self-understanding than a bar graph to describe the observed results.
ANSWER: The graphics was changed as suggested by the reviewer

â€¢ Please, describe your literature search method before to conclude that there is no peer-reviewed journals. Do you have also access to EMBASE or other sources of information other than Med-Line?
ANSWER: The statement about effect of maca on learning in databases has been deleted.

â€¢ Please, attenuate the statement of women cognitive dysfunction after menopause: as it is reported it could appear that all women risk to become demented after menopause.
ANSWER: The statement has been modified as suggested by the reviewer.

â€¢ How can Authors exclude that the observed results are not only the effect of an unspecific Maca improving action on physical performances? Please discuss shortly your opinion about it in the discussion session
ANSWER: This is not discarded and we have included and statement in the discussion.

Discretionary Revisions (which the author can choose to ignore)
ANSWER TO REVIEWER 2:

Reviewer's report
Effect of three different cultivars of Lepidium meyenii (Maca) on learning Title: and depression in ovariectomized mice
Version: 3 Date: 9 May 2006
Reviewer: Shrinivas SK Kulkarni

Reviewer's report:

The authors have observed the effect of three different cultivators of Lepidium meyenii (Maca) on learning by using water finding task and depression by using forced swim test in mice. However, there are certain shortcomings that need clarification.

1. What was the weight of the animals that were used in the present study? Authors have measured the weight of the uterus in milligram only. Generally, the organ weights are always calculated as mg or g organ weight/kg of the body weight comparison with each other.

**ANSWER.** In all of our experiments the body weight was recorded. Body weights were similar between groups. As reported previously, we do not find changes in body weight as compared with control when animals were treated with maca. Therefore, uterus weights or uterus weights/Kg body weights produced a similar profile. For such reason we used the absolute weights.

2. What was the route of administration of ketamine-xylazine anesthesia? Whether these two solutions were mixed in the same syringe or administered separately.

**ANSWER:** The solutions were mixed in the same syringe. They were administered by intraperitoneal route.

3. Have the authors carried out prior randomization of the animals before carrying out the experiments.

**ANSWER:** Yes, mice were randomized previously to the start of the experiments.

4. At what time of the day experiments were carried out.

**ANSWER:** In the first experiment, memory was assessed using the water finding task on days 21 (from 9:00am to 2:00pm) and 22 (from 10:00am to 2:00pm). Forced swimming test was performed 24 hours after the last administration of vehicle or Maca (day 22). These statements were added to the manuscript (Materials and Methods).

5. What was the mortality rate in the present study?

**ANSWER:** No animals died by effect of maca treatment.
6. How the dose selection was done as 1g/kg/day for 21 days. What was the LD50? Maca has been reported in the scientific literature to have a low degree of acute oral toxicity in animals.

**ANSWER:** One g/Kg/day represents almost 50-60 kg in a woman. This dose is almost used by natives at the central Andes in Peru (Valerio & Gonzales, 2005). We used 21 days of treatment since our clinical trial in humans showed that maca reduced scores in tests for depression at 28 days but not after 14 days of treatment. For such reason we tried to demonstrate if an intermediate value of 21 days may be useful as model to study memory and depression. LD50 in our laboratory was higher than 15 g/Kg/day.

7. Why Maca was administered nasogastrically than oral route of administration. This may be discussed.

**ANSWER:** This was a misunderstanding in the manuscript. We have used the oral route by gavage to administer maca. We have clarified in the revised version.

8. Any biological study needs the use of standard reference drug for comparison of the effect on learning and antidepressant activity. Without this data the validity of the test procedure is questionable.

**ANSWER:** One of the limitations of the study is the lack of use of standard reference drug. This will be included in the discussion.

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Declaration of competing interests:**
'I declare that I have no competing interests'