Lepidium meyenii (Maca) does not exert direct androgenic activities

P. Bogani a, F. Simonini b, M. Iriti c, M. Rossoni d, F. Faoro e, A. Poletti b, F. Visioli e,∗

a Department of Pharmacological Sciences, University of Milan, Via Balzaretti 9, 20133 Milan, Italy
b Institute of Endocrinology, Centre of Excellence for the Study and Treatment of Neurodegenerative Diseases, University of Milan, Via Balzaretti 9, 20133 Milan, Italy
c Plant Pathology Institute, University of Milan, Italy
d Department of Plant Production, University of Milan, Italy
e Plant Virology Institute, National Research Council (CNR), Italy

Received 26 May 2005; received in revised form 14 September 2005; accepted 22 September 2005
Available online 18 October 2005

Abstract

Maca is the edible root of the Peruvian plant Lepidium meyenii, traditionally employed for its purported aphrodisiac and fertility-enhancing properties. This study aimed at testing the hypothesis that Maca contains testosterone-like compounds, able to bind the human androgen receptor and promote transcription pathways regulated by steroid hormone signaling.

Maca extracts (obtained with different solvents: methanol, ethanol, hexane and chloroform) are not able to regulate GRE (glucocorticoid response element) activation. Further experiments are needed to assess which compound, of the several Maca’s components, is responsible of the observed in vivo effects.

© 2005 Elsevier Ireland Ltd. All rights reserved.

Keywords: Maca; Lepidium meyenii; Androgen receptor

1. Introduction

Lepidium meyenii, also known as “Maca”, belongs to the plant family of Brassicaceae and was discovered more than 2000 years ago in the highlands of central Peru (Balick and Lee, 2002). Ethnobotanical surveys demonstrate that Maca was widely used during the precolonial and colonial periods of Peru under the Spaniards, who first described of the plant and its properties (Zheng et al., 2000).

Maca roots are edible and rural traditions praise their positive effects on human fertility and their high nutritional value. Today, Maca is thought to be useful in the treatment of depression, cancer, menstrual and sexual disorders as well as for memory dysfunction (Balick and Lee, 2002). However, these claims have rarely been validated by experimental data. Some studies have already been conducted in vitro, to identify the active components of this plant (Zhao et al., 2005), and in vivo to demonstrate the effects of Maca in rats and humans (Gonzales et al., 2002; Eddouks et al., 2005). These studies have found that Maca extracts exert interesting biological activities and contain compounds whose activities are similar to those of testosterone. Actually, serum testosterone levels are directly related to sexual desire (Gonzales et al., 2004), but data in the literature suggest that testosterone should not be used to improve sexual desire in men with normal serum concentrations, because of its effects on the development of prostate cancer (Nelson and Witte, 2002). Other studies (Zheng et al., 2000; Cicero et al., 2001) indicated that oral administration of Maca improves sexual performance, without changing reproductive hormone levels (Gonzales et al., 2005).

Thereby, the hypothesized correlation between Maca intake and fertility still requires biochemical confirmation. For this reason, we have tested the effects of different Maca extracts (obtained with different solvents: methanol, ethanol, hexane, and chloroform) on a gene reporter regulated by androgens.
2. Materials and methods

2.1. Plant material

A voucher specimen of Maca (Lepidium meyenii Walp.) has been identified, classified, and deposited in the herbarium of the Section of Systematic Botany, Department of Biological Sciences, University of Milan, by professor Giuseppe Patrignani.

The powdered tuber (50 g) was extracted with either chloroform, methanol, ethanol, or hexane (150 ml), at room temperature for 1.5 h. The extracts were brought to dryness under nitrogen. After resuspension in a known volume, the content of the extracts was quantified by microgravimetry. Following further evaporation, the extracts were resuspended in DMSO to a final concentration of 100 μg/μl.

2.2. Luciferase and β-galactosidase assay

Androgen-independent prostate cancer cells DU145 were plated into 24-well plates at 300,000 cells/ml, 1 day before transfection. The cells were transiently transfected with 0.5 μg/well of a plasmid containing a glucocorticoid response element (GRE), controlling luciferase gene, 0.19 μg/well of a plasmid codifying for the human androgen receptor (pCMV-hAR), 0.03 μg/well of a plasmid used to evaluate transfection efficiency (pEGFP-N1), and 0.25 μg/well of β-galactosidase expression vector (pCMV/β).

Three hours after transfection, samples were incubated with Maca extracts to a final concentration of 1, 10, and 50 μg/μl. Medium was replaced after 24 h with RPMI 1640 (Biochrom KG, Berlin, Germany) supplemented with 5% charcoal-stripped FCS (CS-FCS), to remove any possible effects of the endogenous hormones found in calf serum, and the treatments were repeated.

For the luciferase assay, the medium was replaced with 150 μl RPMI/well and the reaction was stopped by adding 150 μl/well of luciferase cell lysis reagent (Perkin-Elmer, Wellesley, MA, USA). Luciferase activity was determined as luminescence counts per second (LCPS). β-Galactosidase assay was used to normalize the results (Dondi et al., 2001; Scaccianoce et al., 2003).

2.3. Statistical analysis

Data are reported as means ± standard error of the mean (S.E.). Statistical analysis was performed using the ANOVA test, to compare control values with all treatments. A p < 0.05 was considered statistically significant.

3. Results and discussion

Lepidium meyenii is the only cruciferous vegetable (Brassicaceae family) native to the Americas. The tuber is the only plant organ employed in human nutrition (Dini et al., 1994). The effects of Maca consumption on human reproductive potential, i.e. significantly enhanced libido and spermatogenesis, led many authors to hypothesize pharmacological actions of Maca (Zheng et al., 2000; Cicero et al., 2001; Cicero et al., 2002). Indeed, the chemical composition of Maca tuber includes an array of secondary metabolites arising from different pathways, namely glucosinolates, phenylpropanoids (polyphenols), isoprenoids (monoterpenes and sesquiterpenes), and alkaloids (Dini et al., 2002; Piccione et al., 2002; Sandoval et al., 2002; Tellez et al., 2002; Gonzales et al., 2005). Much research has been published, in recent years, to show how Maca interacts with its target in vivo and in vitro (Cicero et al., 2001; Gonzales et al., 2003; Zhao et al., 2005). At present, it is not clear whether the effects of Maca are due to direct actions of its components on selected cells or to indirect, namely central effects. The aim of this study was to determine if Maca extracts bind the androgen receptor and, hence, carry the potential to directly stimulate spermatogenesis and sexual activity. We used various solvents to extract Maca, because of the different biological activities reported for its different fractions (Cicero et al., 2002). However, even though activation of the GRE (an enhancer sequence activated by AR) was, as expected, greatly stimulated by 17β-estradiol (E2) and 17β-estradiol (E2) activated by dihydrotestosterone in prostate DU145 cells, none of the Maca extracts (1, 10, and 50 μg/μl) were able to activate AR-mediated transcription (Fig. 1). Therefore, our data exclude a direct effect of Maca on genes regulated by androgens. It has also been postulated that the Maca effects on fertility and sexual desire might be modulated by the hypothalamic-pituitary axis, through regulation of hormone secretion, but studies performed on humans and animals have demonstrated that treatment with Maca does not affect serum reproductive hormone levels (Gonzales et al., 2002).

Recently, a metabolite of the aromatic glucosinolates was described as a specific antagonist of the androgen receptor; therefore, it is possible that the effects of Maca are due, at least in part, to interactions between glucosinolates and the androgen receptor (Le et al., 2003). Also, it is conceivable that Maca contains phyto-estrogens: the potential role of phyto-estrogens on human male fertility has been attributed to both estrogenic or anti-estrogenic activities (Roche et al., 2001). Indirect effects of Maca, on the other hand, can be consequent to its anti-stress properties.
and anti-depressive properties, as hypothesized by Gonzales et al. (2003).

In synthesis, our study shows that Maca does not modulate androgen receptors (Fig. 1). Therefore, although there is evidence associating enhanced sexual libido, fertility, and spermatogenesis with Maca consumption, a pharmacological and causal relationship between Maca ingestion and its effects on human reproduction is yet to be ascertained, in order to identify the mechanisms of action of Maca components. Further, chemical and molecular research is needed to identify which of the many Maca components is responsible for the observed effects. Finally, in vivo experiments are to be undertaken, to confirm the possibility of using Maca supplementation as a tool to improve fertility (Cicero et al., 2001).

Acknowledgement

We thank Ecomundo (Lima, Peru) for the supply of Maca.

References


