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For Chapter in Books:
López de Almeida JM. (2000). Formulación farmacéutica de productos fitoterapéuticos, pp 113-124. En Sharapin, N: Fundamentos de tecnología de productos fitoterapéuticos. Ed. CAB y CYTED, Bogotá, Colombia.

According to Ramón and Cajal: the people that wants to write a scientific article, should have three requirements: 1) to have something to say; 2) to say it; and, 3) not to say nothing else that that. (taken of Bol. Soc. Chil. Quím.).

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MACA *Lepidium meyenii*

ANTONIO BIANCHI[3]

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A MORE COMPLETE FOOD THAN ROYAL JELLY

"This plant grows in the harshest
and coldest areas of the sierra,
where no other plant for man's
sustenance can be grown"
Father Bernabè Cobo 1653

Who has ever seen the puna? An enormous and infinite cold desert. No trees, no flowers, only small clumps of dried grasses. A blue cold that takes your breath away, some puddles of stagnant water, an inert silence. At night, when the temperature falls well below zero, the twinkling of the stars is transformed into a cascade of light "Puna brava, Puna dura", say the Peruvians. A desert of absolute cold surrounded by snow-covered peaks, a few huts with stone walls and thatched roofs and a gelid cold that penetrates right into your bones. The sun is there, immobile and distant at the same time, indifferent and sluggish in an absence of heat. It is in this hostile and distant environment that the small potato of the Andes grows, the secret of the ancient Inca, the Maca. Scientists call it *Lepidium meyenii*: actually not all of them, but the majority now agree that this is the real scientific name.

HISTORY

Its cultivation was once very common in many parts of the Perù and Bolivia plateau: the area of Huancavelica, Ayacucho and the department of Puno still have place-names such as "Macapata", "Macapampa" or "Macachacra" (1). Today it grows only in a few parts corresponding to the ecological regions of Suni y Puna, on the shores of Lake Chinchapoya, in the department of Junin and Pasco, at an altitude of between 3700 and 4450 metres above sea-level. In total, less than 50 hectares are devoted today to the cultivation of this foodstuff (2). How has such a drastic reduction in the area of cultivation come about?

From prehistoric remains it is now confirmed that the first inhabitants of the Peruvian plateau knew the Maca: between 4000 and 1200 BC an agriculture based on the domestication of the "papa shillinco" of the Maca and of the Oca" was born. But it was the birth of the Cusco and the Inca civilization that fully exploited this tuber The Inca soldiers were fed with rations of Maca to increase their strength and physical performances in extenuating marches and fierce combats. Some writers (3) have even gone so far as to hypothesize that the ascent of this civilization could in some way be related to a diet based on this foodstuff.

The reason for the impressive restriction of the area of growth of Maca is mainly due to the progressive depletion of the soils (4). Maca, a foodstuff that is very rich in nutrients, is believed to progressively exhaust the soil. Therefore a system of cultivation by rotation is necessary, with a period of fallow for the soils of 5-10 years, but even with this system, with the passing of the years, the number of areas that can be cultivated progressively decreases. After centuries, Maca only grows now in a relatively small area of the Perù and this is despite research by the Instituto Nacional de Investigacion Agraria y Agroindustrial (INIAA) which has repeatedly tried to extend these cultivations.(5).

BOTANY

The first description of the maca was the merit of Dr.G. Walpers in 1843 who used a specimen from the department of Puno and coined the term *Lepidium meyenii* Walp. This description remained

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unquestioned until 1989 when Gloria Chacon proposed the distinction between *Lepidium meyenii* and *Lepidium peruvianum* Chacon, stating that only the latter is the legitimate maca (6). The work of this author was based on a cultivated specimen from the city of Cerro de Pasco, department of Pasco. In fact, this distinction has not had any particular follow-up today and all Authors today speak exclusively of the *Lepidium meyenii* as the only maca existing in nature, considering the term *Lepidium peruvianum* a synonym. From the botanical point of view, the maca corresponds to:

DIVISION	ANGIOSPERMAE
CLASS	DICOTYLEDONEAE
SUBCLASS	ARCHICHLAMYDEAE
ORDER	PAPAVERALES
FAMILY	BRASSICACEAE
GENUS	*Lepidium*
SPECIES	*Lepidium meyenii*
COMMON NAME	MACA

Reference (3)

The Brassicaceae family consists of over 2500 species and over 350 genera, including very important vegetables such as broccoli and cauliflower. The term Lepidium derives from the Greek “Lepidion”, which literally means “small scale”, the name given by Dioscorides to small fruit of this genus. This is a cosmopolitan genus which includes about 130 species in the world: in Peru alone there are 15 species (7).

The maca appears essentially in the vegetative phase as a small rosette of leaves, which becomes larger in the generative phase when it is made up of leaves and flowers, and by a root generally of a conical shape, which is its underground organ and which can reach a length of about 18 cm and a diameter of about 6.5 cm. The dimensions can in fact vary a great deal, with very small specimen
s which reach 1 cm. in length and 0.6 cm. in diameter. Medium sizes are generally around 5-6 cm long and 3-5 cm wide.

The latter are those generally most appreciated by the Indian populations. The larger ones on the other hand, are too rich in fibre and are considered of poor nutritional value and called “shugla”. The colour of the root varies from plant to plant, ranging from light yellow to dark red and even brown-black: there exists a vast native classification of the different species which are not necessarily in relation to their quality, as shown by modern chemical studies. From a recent study carried out on 758 plants from the department of Junin, the following 13 ecotypes were found:

Colour of the root	Percentage of ecotypes
Yellow	47.8%
Red-white	16.5%
Scarlet red-white	9.0%
White-red	6.3%
Lead grey	5.4%
Black	4.2%
Red-yellow	3.7%
White	2.2%
White- scarlet red	1.6%
Yellow-red	1.3%
Light lead grey	0.8%
Scarlet red-lead grey	0.7%
Yellow-light lead grey	0.5%

Reference (3)

PHYTOCHEMISTRY

As far as the chemical composition of maca is concerned, we have to distinguish two major categories: the primary compounds (of a nutritional nature) and the secondary ones. Nutritional studies on the maca have obviously revealed a considerable difference in the content of macroinutrients. In 1968 Gloria Vasquez, in her doctoral thesis, reported for the first time the following composition (9):

Chemical composition	Percentage
Humidity	35.51 g%
Total nitrogen	1.71 g%
Proteins	10.30 g%
Lipids	26.10 g%
Carbohydrates	24.63 g%
Ashes	3.46 g%
Calcium	207.90 mg%
Iron	9.93 g%
Phosphorus	328.10 mg%
Calories	384.00 Kcal

Reference (3)

This study reveals an optimum protein content and an appreciable content of calcium and iron, which make this foodstuff indicated in many states of deficiency. In 1973 another thesis (9) appeared which in part confirms and in part scales down the previous data, reporting the following:

Chemical composition	Percentage
Major components	
Water	68.70%
Proteins	3.80%
Lipids	0.60 g%
Carbohydrates	23.00 g%
Ashes	1.40 g%
Calories	176.00 kcal

Vitamins	
Carotene	0.07 mg
Thiamine	0.15 mg
Riboflavin	0.31 mg
Ascorbic acid	3.10 mg
Minerals	
Calcium	94.00 mg %
Phosphorus	57.00 mg %
Iron	2.20 mg %

Reference (3)

The results of this second study show a protein, lipid and iron content that is significantly less than the first and a calcium content that is still very appreciable. The difference in the results is probably to be derived from the different typology of specimens analysed. The larger potatoes, even if aesthetically better, are in fact rich mainly in fibre and therefore are of a low caloric and nutritional value, whilst the smaller ones have more macronutrients. A recent thesis at the University of San Marcos (10) has tried to put some order in the subject, focusing its interest on specimens that the farmers consider suitable for human consumption.

Major compounds	**Yellow variety (g %)**	**Red variety (g %)**	**Black variety (g %)**
Humidity	9.71	10.14	10.47
Total proteins	17.99	17.22	16.31
Fats	0.82	0.91	0.82
Fibres	5.30	5.45	4.95
Ashes	3.49	3.68	3.63
Carbohydrates	62.69	62.60	63.82
Total nitrogen	2.87	2.76	2.42
Non-protein nitrogen	1.55	1.16	1.36
Pure protein (NP x 6.25)	8.25	9.97	7.7
Starch	37.86	37.52	38.18
Soluble sugars Direct reducers	6.17	6.03	7.02
Soluble sugars Indirect reducers	16.52	17.26	17.10
Vitamins	**Yellow variety (mg %)**	**Red variety (mg %)**	**Black variety (mg %)**
Niacin	43.30	37.27	39.06
Ascorbic acid	3.52	3.01	2.05
Riboflavin	0.61	0.50	0.76
Thiamine	0.42	0.52	0.43
Minerals	**Yellow variety (mg %)**	**Red variety (mg %)**	**Black variety (mg %)**
Potassium	1130	1160	1000
Sodium	20	20	40
Magnesium	70	80	80
Calcium	190	200	240
Phosphorus	320	290	280
Trace elements	**Yellow variety (ppm)**	**Red variety (ppm)**	**Black variety (ppm)**
Copper	6	6	8
Zinc	32	30	30
Manganese	22	20	22
Iron	80	62	86
Boron	12	24	26

Reference (3)

This last study, as well as confirming the concerns on the quality of the maca put on to the market, nevertheless reveals how maca has a very respectful protein content, especially if related with the low levels of fat. The fats of the maca are lower than that of the potato (1.8%), kiwicha (2.5%) or maize (3.9%). The presence of a discreet carbohydrate fraction nevertheless makes maca a foodstuff that, although reduced (comprised between 176 and 384 Kcal) is not without caloric value. This factor makes it an ideal complement in the athlete's diet (rich supply of protein, few fats but with a discreet energy supply in terms of calories). This value is increased further if we analyse in particular the type of amino acids present in this Andean tubercle (11):

Amino acids	**Concentration in mg/g of protein**
Glutamic acid	156.5
Arginine	99.4
Aspartic acid	91.7
Leucine	91.0
Valine	79.3
Glycine	68.3
Alanine	63.1
Phenylalanine	55.3
Lysine	54.5
Serine	50.4
Isoleucine	47.4
Threonine	33.1
Tyrosine	30.6
Methionine	28.0
HO-Proline	26.0
Histidine	21.9
Sarcosine	0.7
Proline	0.5
Cystine	not determined
Tryptophane	not determined

(essential amino acids in bold type),
Reference (3)

Practically all the essential amino acids, apart from tryptophane, are present. This data is also confirmed by subsequent studies (12):
Content in essential amino acids of the maca.

Amino acids	G/100g of protein
Isoleucine	4.3
Leucine	6.8
Valine	6.3
Lysine	5.8
Phenylalanine + Tyrosine	4.8
Threonine	4.5
Methionine + cystine	3.3

The maca is therefore an ideal food for the athlete, precisely due to its richness in those nutrients essential for the development of a muscular mass that is adequate to sustain considerable and, above all, prolonged, effort. This obviously does not mean that we have in front of us the concentrations which certain "gym" supplements have made us used to, with great concern for safety and perplexity for their real effectiveness. The position of maca as a dietary supplement is more diversified and in a certain sense, more "complete". It contains in the correct dietary concentrations, all the nourishment required by a person subjected to intense physical effort (such as a peasant obliged to work for 8 – 10 hours at over 4,000 metres above sea-level). In addition, the energizing action of the maca is not limited to its nutritional value. Experiments on rats have shown that taking maca in alimentary doses can increase the levels of glucose in hypoglycaemic rats after a prolonged fast (18hours) or after pharmacological induction (insulin): this data is particularly significant as it shows an action of glucogenesis, the production of glucose from the reserves of glycogen in the organism (13). The availability of glucose is put into relation with the energy reserves of the organism and the hypoglycaemic crisis is the first sign of the "collapse" of athletes subjected to prolonged effort. The utility of the maca for the athlete is therefore particularly indicated for those who are seeking an improvement in their physical resistance and in prolonged effort.

The concentration of relevant doses of minerals (11) make it more useful for this purpose.

Minerals	mg/110 g of dry plant
Iron	16.6
Manganese	0.8
Copper	5.9
Zinc	3.8
Sodium	18.7
Potassium	2050.0
Calcium	150.0

The presence of significant concentrations of iron and calcium also make it suitable to supplement all those situations of increased requirements, especially in women: pregnancy and ageing, above all. In particular the concomitant presence of high concentrations of these minerals and of all the essential amino acids necessary for the growth of the foetus make it an excellent source of nutrition during pregnancy, as reported by the Andean tradition knowledge. Naturally on condition that significant doses are reached, corresponding to about 5-10 g per day. On the other hand, its highly publicised use as a slimming supplement leaves us perplexed. Given its low but not negligible caloric value, the maca can represent an interesting foodstuff for slimming diets on condition that it is part of the daily calorie count: otherwise its use as an additional supplement risks altering the real calorie supply, compromising the result of the diet.

THERAPEUTIC ACTIVITY

As far as the secondary compounds currently identified in the maca are concerned, these are essentially of three categories:

- **COMPOUNDS OF A STEROID NATURE**

These include the following compounds (11):

Steroid compounds	Percentage
Sitosterol	45.50%
Campesterol	27.30%
Ergosterol	13.60%
Brassicasterol	9.10%
Ergostaniedol	4.50%

At the state of present knowledge and of the concentrations of these compounds present in the maca,. none of these components appear to be able to exercise a significant action on the properties of this foodstuff.

- **AROMATIC GLUCOSINOLATES**

The maca contains isothiocyanates of an aromatic nature already shown in many other Brassicaceae. Between these glucotropaenoline and m-methoxyglucotropaeoline have been shown in particular (13). These compounds seem to have preventive activities on many models of tumours (especially of the gastrointestinal system) on experiment animals. It must however be specified that the concentration of these substances is much higher in foodstuffs closer to our dietary tradition (Brussels sprouts, broccoli etc.) therefore it appears decidedly illogical to use the maca to seek this chemical-preventive effect.

- **ALKALOIDS**

Four alkaloids have been identified in the maca (3): macaine 1,2,3 and 4. The presence of these compounds has been put into relation with the aphrodisiac and anti-sterility activity of the maca but to date scientific proof is lacking in order to support this function.

- **POLYUNSATURATED FATTY ACIDS: THE PROBLEM OF THE ACTIVE INGREDIENTS.**

The maca has, in traditional Andean medicine, an aphrodisiac and anti-sterility function. Altitude has in fact a strongly inhibiting action on sexuality and on the reproductive capacities of man and animals. The Andean peoples have always maintained that a diet based on the maca can contrast this effect. This action has been shown today in some experiments on farm animals. Regularly taking maca induces an increase in sexual relations and an increase in the Graaf follicles in the female animals, whilst in male animals the volume of seminal fluid is increased by 20%, sperm motility by 40% and the number of spermatozoids by 33%: all this can be translated in the end by a larger number of pregnancies brought to term (3). To reach these objectives the percentage of maca flour in the diet should correspond to about 6%. The limit of these studies mainly consists of the absence of a control group. This effect has subsequently been the object of at least four studies on animals (with a relative control group) which have at least confirmed the aphrodisiac effect. On the basis of this research it is probable that the active fraction is that regarding the polyunsaturated fatty acids; amongst these, two in particular take on particular importance, macaene and macamide (15). However, the presence of these compounds varies enormously in the various products on the market, oscillating between 0.15% and 0.84%, with the result that the consumption of these compounds oscillates between 1-52 and 14.88 mg/die (16). Other Authors had hypothesized in this sense a role of the isothiocyanates (1) or the steroid substances (11).

CLINICAL STUDIES AND EXPERIMENTAL PHARMACOLOGY

Two studies have been carried out in Italy, one in China and one in Perú. Two studies were carried out by the University of Modena. In the first, it was shown how the aphrodisiac effect, on experiment rats- visible through an increase in copulative performance, is independent of the nutritive value of the maca (17). In the second however, it was shown how above all the hexanic extract is responsible for this and not the chloroform extract (17). The Chinese study showed how by supplementing the diet of experiment rats with such an extract at 10% for 22 days there was, in the group treated, an increase in the number of sexual intromissions that was four times greater and an increase in the number of females positive with the presence of sperm of 2.5 times. (18). Whilst a Peruvian study showed that an aqueous extract of maca (66.7 mg/ml) given for 14 days results in an increase in the weight of the testicles and of the epididymis, with an increase in the number of mature spermatozoids (19).The last two studies essentially maintain how the use of maca has as a primary indication male sterility rather than a simple aphrodisiac effect and this action, from a therapeutic point of view, would without doubt be more fascinating and in tune with traditional Andean medicine. It must be underlined that a recent Peruvian study has shown how taking tablets of maca (1500-3000 mg/die) for four months led in nine subjects aged between 22 and 44 to an increase in seminal volume, in spermatozoid count and an increase of sperm motility and the number of mobile spermatozoids. None of these effects was in any way traceable to a hormone-mediated action due to an increase in luteinizing hormone, stimulating follicle, to an increase in prolactin, testosterone of estradiol (20). Given the worrying risks in the long term connected with an increase in these hormones, this is no meagre result.

The primary interest of maca for anti-sterility and possibly as an aphrodisiac (even if in this case we are still far from clear evidence) lies precisely in the fact that it seems to depend on compounds that contribute in some way to its food value. That is, it would be a question of natural substances with a wide safety margin (tests on animals have not shown any sign of toxicity at doses of 3 g/kg) which make maca a completely different aphrodisiac from substances such as ginseng, muira puana or yohimbina, for which (in the absence of equally clear evidence) there always exists the danger of side effects. Maca is a natural foodstuff that can be used for long periods and with an excellent margin of safety: the Andean peoples have been using it for thousands of years at high doses without any sign of toxicity having been shown.

PRODUCTION AND USES

As mentioned earlier, there exists a serious problem of availability of ground for maca: the Andean populations have consequently developed over the centuries a refined technology to maximise as far as possible the preservation of the beneficial properties of this foodstuff. The traditional method of preparation appears to consist of a slow drying of the fresh potatoes which takes from six to eight weeks. During the day the maca is spread out on special sacks and exposed to the sun of the Andes: it is

gathered in the evening in order to protect it from the night freezing and exposed again the next day. Drying in the sun modifies the taste, making it more pleasant, perhaps degrading the fraction of glucosinolates or hydrolyzing the fibre content. At this point only the smaller potatoes are selected, as they are poor in fibre and richer in nutritive substances. The larger ones are kept as animal fodder. The pressure exercised by the commercial success in recent years of maca-based products today risks modifying this traditional system of production. There have been cases where the maca potatoes have been put on to the market without considering their dimensions and often dried quickly in rudimentary ovens. Even the Institute for the Study of Genetic Resources of the FAO in Rome intervened on the matter and which, in collaboration with the prestigious Centre for the Study of the Potato of Peru, set up a specific programme to protect the quality of maca put on to the market and to promote organic cultivation, free of chemical additives.

Today the advice for those who wish to use maca as an energizing foodstuff is without doubt that of using the flour or the whole potato: modern research has shown that this is the best way to preserve all the nutritive elements. Moreover, no research exists to date that has been able to isolate a fraction responsible for the energizing or anti-hypoglycemizing activity. The matter of the aphrodisiac properties is more complex: in this case, the experiments available would give more evidence for the use of extracts that exploit the presence of polyunsaturated fatty acids: different preparations, mainly in the form of capsules. are present on the European and American markets. Three thousand years on, the small potato from the Andes never ceases to amaze.

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ARTICULO 2 (ARTICLE 2)

BUDDLEJA GLOBOSA: A MEDICINAL PLANT OF CHILE, THEIR CHEMISTRY, BIOLOGICAL ACTIVITY AND TRADITIONAL USES

PETER J. HOUGHTON[4]

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ABSTRACT: *Buddleja globosa* has been found to contain flavonoids, phenylethanoids, iridoids, sesquiterpenes, diterepens and triterpenoids. In vitro tests have shown that the flavonoids and phenylethanoids have activities related to the traditional use of the leaves for wound healing and for liver ailments. The sesquiterpenoids present have antifungal properties and anti-inflammatory properties and an extract has shown antiplasmodial activity which warrants further investigation to determine the compounds responsible.

Resumen: En *Buddleja globosa* se ha encontrado que contiene flavonoides, feniletanoides, iridoides, sesquiterpenos, diterepenos y triterpenoides. En análisis in vitro se ha mostrado que los flavonoides y feniletanoides tienen las actividades relacionadas al uso tradicional de las hojas para la curación de las herida y para las dolencias más fuertes. Los sesquiterpenoides presentes tiene propiedades antihongos y propiedades antiinflamatorias y un extracto ha mostrado actividad antiplasmodial que garantiza la investigación extensa para determinar los compuestos responsable.

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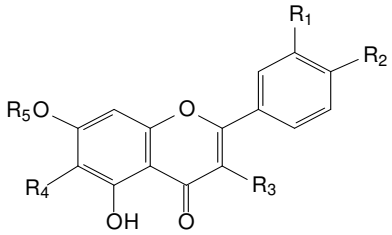
INTRODUCTION

The genus *Buddleja* (Buddlejaceae) is sometimes named *Buddleia* in the scientific and popular literature and previously was included in the Loganiaceae. *Buddleja globosa* Hope is a bush attaining 4m in height which is common in the central and southern regions of Chile and also in similar areas in Argentina, Bolivia and Peru. It is widely grown as an ornamental in parks and gardens in the United Kingdom because of its globose heads of golden-yellow flowers which attract large numbers of honey bees in early summer. *B. globosa* is known in Spanish as 'matico' and as 'palñin' or 'pañil' in the language of the Mapuche, the indigenous inhabitants of central Chile, and as 'palguin' in Quechua (1,2). The leaves of the plant were official in the first Chilean Pharmacopeia (1886) and an infusion of the leaves was used for washing wounds while the powdered dried leaves were used to heal ulcers and old wounds (1,2). An infusion of the leaves was drunk to treat chronic dysentery, haemorrhoids, hepatitis and catarrh. The juice of the leaves was also used to treat warts and callous ulcers(1). These uses in traditional medicine are very similar to those for other *Buddleja* species from central America, southern Africa and eastern Asia (1).

CHEMICAL CONSTITUENTS

B.globosa contains a variety of compounds including flavonoids **1- 6**, phenylethanoid esters **7,8** and terpenoids including iridoids, sesquiterpenes, diterpenes and saponins:



Structure 1 = Luteolin				
R_1 = OH	R_2 = OH	R_3 = H	R_4 = H	R_5 = H
	Reference 3			