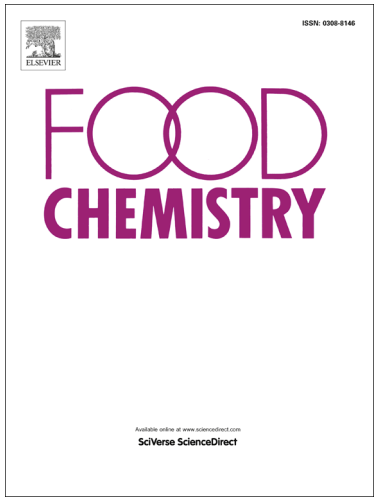

Chemical composition and health effects of maca (*Lepidium meyenii*)

Sunan Wang, Fan Zhu

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Chemical composition and health effects of maca (*Lepidium meyenii*)

Sunan Wang [a,b], Fan Zhu [b,*]

[a] *Canadian Food and Wine Institute, Niagara College, 135 Taylor Road, Niagara-on-the-Lake, Ontario, LOS 1J0, Canada*

[b] *School of Chemical Sciences, University of Auckland, Private Bag 92019, Auckland 1142, New Zealand*

[*] *Correspondence, email: fzhu5@yahoo.com*

Abstract

Maca (*Lepidium meyenii* Walpers) has emerged as a popular functional plant food due to various claimed health effects. This review details the major (i.e., starch, dietary fiber, and protein) and minor constituents (i.e., minerals, non-starch polysaccharides, polyphenols (flavonolignans), macaenes, macamides, glucosinolates, and alkaloids) of maca (root and aerial parts). Diverse health effects of maca are also summarized. Various bioactivities of maca include enhanced reproductive health, antifatigue, antioxidation, neuroprotection, antimicrobial activity, anticancer, hepatoprotection, immunomodulation, and improving skin health and digestive system's function. Plant genetics, botanical parts, processing, extraction, and experimental protocols represent the major factors affecting the chemical composition, physicochemical attributes, and health effects of maca-based products. However, clinical studies to support the claimed health effects of maca and related mechanisms appear to be lacking. Product innovation and diversification in food and non-food utilization of different parts of maca to maximize the value perceptions are suggested.

Keywords: *Lepidium peruvianum*; chemical analysis; bioactivity; antioxidant; health-promoting; underutilized species

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Abbreviations

AChE: acetylcholinesterase
AR: androgen receptor
Ara: arabinose
BuChE: butyrylcholinesterase
ED: effective dose
FAAH: fatty acid amide hydrolase
FTIR: Fourier-transform infrared spectroscopy
Glc: glucose
Gal: galactose
Man: mannose
MPTP: tetrahydropyridine
PSA: prostate-specific antigen
RDAs: recommended dietary allowances
Rha: rhamnose
Rib: ribose
TCT-GC/MS: thermal-desorption cryo-trapping-gas chromatography-mass spectrometry
TG: total triglycerides
UV: ultraviolet
Xyl: xylose

1. **Introduction**

Maca (*Lepidium meyenii* Walpers) (*Lepidium peruvianum* is a synonym) became domesticated probably between the years 4000–1200 BCE at the high plateaus of the Peruvian central Andes (Toledo et al., 1998). This biennial herbaceous plant belongs to the cruciferous (Brassicaceae) family which also includes cauliflower, cabbage, and garden cress (Toledo et al., 1998). Maca grows in altitudes varying between 2800 to 5000 m above sea level. The plant adapts well to extremely harsh high altitude conditions (cold, strong UV radiation, low oxygen level, and capricious climate) (Zhang, Tian et al., 2016). Peru is a leading maca producer. The major consumer countries of maca based products include USA, Canada, UK, Germany, China, Japan, and the Netherlands (Meissner, Mscisz, Kedzia, Pisulewski, & Piatkowska, 2015). Maca

has been adapted to the other parts of the world such as Yunnan Province in China for large-scale cultivation (Chen, Li, & Fan, 2017; Tang et al., 2017).

The edible part of maca is hypocotyls and main tap root, commonly called hypocotyl or root in literature. In this review, it is called root to avoid any confusion. Leaf, stem and inflorescence of maca (termed aerial parts) as a potential source of edible vegetables remain underutilized (Jin, Chen, Huo, Cui, Yu, & Yu, 2018). The maca root can reach approximate 20 cm in circumference, whereas the plant can reach a height of 10–20 cm (Figure 1A). There is a great genetic diversity in morphology of maca roots. This diversity is characterized by different weight (1–5 kg), diverse shapes (spherical, oval, spherical oval, spindle-shaped), and a variety of colors for skin and flesh (white, cream, yellow, orange, red, claret, and purple) (Hernandez Bermejo & Leon, 1994; Brinckmann & Smith, 2004; Lin, Huang, Sun-Waterhouse, Zhao, Zhao, & Que, 2018). The visual features of the most representative maca phenotypes (yellow, red and black maca) are illustrated in Figure 1B (Chen et al., 2017). It would be expected that this genetic diversity may lead to variations in nutritional composition of maca.

Nutritional value of maca root partially lies in its major dietary constituents, which include starch, dietary fiber, and protein (Dini, Migliuolo, Rastrelli, Saturnino, & Schettino, 1994; Chen et al., 2017; Li, Chen, et al., 2017; Rondán-Sanabria, Valcarcel-Yamani, & Finardi-Filho, 2012; Zhang, Li, Wang, Yao, & Zhu, 2017). The leaves are also a source of dietary fibers, minerals, vitamins and essential amino acids (Jin et al., 2018). Minor dietary constituents of maca are believed to be largely involved in various biological benefits. A variety of compounds with pharmacological significance in maca roots and leaves include non-starch polysaccharides, polyphenols (e.g., flavonolignans), malamedas, macaenes, macamides, glucosinolates, and macahydantoins (Li, Ammermann, & Quiros, 2001; Dini, Terone, & Dini, 2002; Muhammad,

Zhao, Dunbar, & Khan, 2002; Cui, Zheng, He, & Zheng, 2003; Zhao, Muhammad, Dunbar, Mustafa, & Khan, 2005; Bai, He, Roller, Lai, Bai, & Pan, 2015; Wang, Wang, McNeil, & Harvey, 2007; Yabar, Pedreschi, Chirinos, & Campos, 2011; Zhang, Wang, Lai, & Wu, 2016; Wang et al., 2016; Zhou et al., 2017; Korkmaz, 2018; Zhou et al., 2018). These components alone or in combination in maca showed an array of bioactivities in model systems, including reproductive health-promoting, neuroprotection, antioxidation, antifatigue, anticancer, hepato-protection, antiosteoporosis, antidysmnesia, and immunomodulation (Zheng et al., 2000; Cicero, Bandieri, & Arletti, 2001; Cicero, Piacente, Plaza, Sala, Arletti, & Pizza, 2002; Gonzales et al., 2002; Valentova, Buckiova, Kren, Peknicova, Ulrichova, & Simanek, 2006; Valentova et al., 2008; Bai et al., 2015; Wang et al., 2016; Tang et al., 2017; Li, Xu, Zheng, Xi, Cui, & Han, 2018; Beharry & Heinrich, 2018; Korkmaz, 2018). However, the information on the health effects of maca is rather scattered. An update of diverse claimed health effects is needed to provide a support for the high exploitation of maca.

Because of the various claimed health benefits, maca derived food products have become popular in niche food market for consumers who are health conscious. Maca have been formulated into a range of commercial products, such as maca root pills or capsules, flour (dried and milled), gelatinized flour (dried, extruded and milled), plain or encapsulated hydroalcoholic extracts, liquor, mayonnaise, chocolate, and tonic drinks (Li et al., 2001; Yabar et al., 2011). Maca based ingredients have great potential as food additives for specific technological functions (e.g., texturizing, antioxidant and antimonial) (Zhang, Li et al., 2017). Despite this potential, very few studies have broached this concept. Innovation of maca based products is necessary to support maca as a sustainable crop.

A previous review on biological and pharmacological properties of maca summarized the literatures from over 10 years ago (Wang et al., 2007). Most recent review articles of maca focused on characterizing non-starch polysaccharides and antioxidants, and pharmacological effects on reproductive health (Li, Xu et al., 2018; Korkmaz, 2018; Beharry & Heinrich, 2018). Focusing the publications from the last decade, the current paper comprehensively overviews the chemical components of maca root and aerial parts. *In vitro* and *in vivo* toxicology and bioactivities of maca are covered. Diverse food and non-food applications of maca are discussed. Novel uses of maca are proposed for improved nutritional quality, sensory attributes, and health–promoting properties of products containing maca. This review provides fundamental knowledge to develop maca as a sustainable crop.

2. **Chemical composition**

2.1. Proximate composition

Chemical composition of maca varied among different reports, depending on crop genetics, pant parts, agricultural practices (e.g., soil, water and climate conditions, and farming practices), postharvest handling (e.g., storage conditions and drying process) and analytical methods used (Table 1). Only a few previous studies focused on comparing the chemical profiles of different parts of maca plant with other commonly used dietary plants, including *Brassica* species and varieties, such as broccoli, cauliflower, cabbage. Limited comparison studies were done on starch (Zhang, Li, Wang, Yao, & Zhu, 2017), dietary fibers (Chen, Zhao et al., 2015), and endogenous enzymes (Rondan–Sanabria et al., 2006) in roots, and vitamin C and niacin in aerial parts of maca (Jin et al., 2018).

2.1.1. Root

Fresh maca root has a water content of over 80%, being a low energy and nutrient-dense food (Dini et al., 1994). The contents of moisture, protein, crude lipid, total carbohydrates and ash of maca roots (cultivated in Peru and China) varied between 4.63 and 10.40 % (wet basis), 9.56 and 21.90 % (dry basis), 0.59 and 2.20% (dry basis), 46.1 and 74.8% (dry basis), and 3.41 and 4.9 % (dry basis), respectively (Dini et al., 1994; Chen et al., 2017; Li et al., 2017).Typically,fresh root is dried for further processing.

2.1.2. Aerial part

The contents of moisture (79.79−88.50 %, wet basis) and protein (23.02−38.48%, dry basis) of maca aerial parts (leaf, stem, and inflorescence) varied at different growth stages, including seedling, reproductive, bolting and flowering stages (Jin et al., 2018).

2.2. Carbohydrate

Carbohydrates are the most abundant in maca roots (~46–74 %, dry weight) (Wang, Zou et al., 2016; Li, Hao et al., 2017; Tang et al., 2017; Li, Xin et al., 2018; Li, Xu et al., 2018).

2.2.1 Root

2.2.1.1. Starch

The starch content of maca root is ~37–77%, similarly to that of sweet potato (Rondán-Sanabria et al., 2012; Wang, Nie, & Zhu, 2016; Zhang, Li, Wang, Yao, & Zhu, 2017). Total starch contents in maca root remained similar during a storage period of 21 days at room temperature (~22 ^{o}C) (Rondán-Sanabria et al., 2012). Starches isolated from three maca roots (yellow, purple and black) contained 0.07–0.10% protein, negligible amounts of lipids, and 159.7–214.0 mg/kg phosphorus. In comparison, potato starch had 0.04% protein and 548.8 mg/kg phosphorus. Cassava starch had 0.16% protein and 57.2 mg/kg phosphorus (Zhang, Li, et

al., 2017). Maca starch granules showed irregularly oval shape and B–type polymorph. Some differences in starch granule sizes (9.0–9.6 μm), apparent amylose content (21.0–21.3%), degree of crystallinity (22.2– 24.3%), onset gelatinization temperatures (47.1–47.5 °C) were observed among starches isolated from yellow, purple and black maca (Zhang, Li et al., 2017). These differences contributed to different pasting and gel texture properties of the starches. Starches from yellow and purple maca had the highest and lowest viscosity, respectively. Starch from black maca had the highest gel firmness (Zhang, Li et al., 2017). Compared to potato, maize, and cassava starches, maca starches had a higher gelation and retrogradation, swelling, water solubility and pasting viscosity, and lower resistance towards shearing (Zhang, Li et al., 2017). Maca amylopectins varied in unit chain length profiles (Zhang, Li, Yao, & Zhu, 2018). Specifically, the average chain length, external chain length and internal chain length of the 3 maca amylopectins were in the ranges of 16.72–17.16, 11.24–11.89, and 4.27–4.48 glucosyl residues, respectively (Zhang et al., 2018). Information is still limited regarding the relations of molecular structures of maca starches to genetic variations, functional properties, and their utilization.

2.2.1.2. Non-starch polysaccharide

Non-starch polysaccharides of maca differed in molecular weight and monosaccharide compositions, which were affected by extraction conditions (Table 2). maca root contained a significant portion of polysaccharides (~10% of the dry weight) (Tang et al., 2017). Maca root polysaccharides were isolated using water (Tang et al., 2017; Li, Sun et al., 2017) and ultrasound–assisted extraction (Zhang, Zhao et al., 2017), which was followed by purification using alcoholic precipitation and resin (ion–exchange column and gel filtration chromatography) (Li, Sun et al., 2017). The monosaccharide composition of the polysaccharides was determined

by HPLC (Li, Sun et al., 2017). Methylation analysis, periodate oxidation–Smith degradation and NMR analysis determined the structures of the polysaccharides (Zhang, Wang et al., 2016).

A polysaccharide fraction MP–1 (1067.3 kDa, 91.63% purity) of maca root contained Rha, GalUA, Glc, Gal, Xyl, and Ara linked by α–glycosidic linkage (Zhang, Zhao et al., 2017). An acidic hetero–polysaccharide fraction (molecular weight, 793.5 kDa) of maca root was made up of D–Gala, D–Glc, L–Ara, D–Man, D–Gal and L–Rha (molar ratio at 35.07:29.98:16.98:13.01:4.21:0.75) (Tang et al., 2017). The backbone of this polysaccharide was consisted of *β*–1,3–Galp (A), *β*–1,3–Glc*p*, and *α*–1, 3–Man*p* residues in a ratio of 5:4:1(Tang et al., 2017). A 7.6 kDa (MPS–1) and a 6.7 kDa polysaccharide (MPS–2) fraction were isolated from hot water (80 °C) extract of yellow maca root (Li, Sun, Meng, Wang, Xiong, & Zhang, 2017). MPS–1 (93.2%) had a higher content of total sugars than MPS–2 (91.5%). The uronic acid content of MPS–1 (1.2%) was lower than that of MPS–2 (26.9%) (Li, Sun et al., 2017). MPS–1 was made up of Xyl, Ara, Gala and Glu (a molar ratio of 1:1.7:3.3:30.5). MPS–2 was made up of Ara, Gal, and Glu (a molar ratio of 1:1.3: 36.8) (Li, Sun et al., 2017). MPS–2 contained α-and β-pyranose, while MPS–1 only had α–pyranose. A hetero–polysaccharide (MCP) of a water extract of maca root was made up of Rha, Glc and Gal at a molar ratio of 2.34:10.21:1.00 (Li, Xin et al., 2018). MC–1 was made of Ara, Man, Glu and Gal at a molar ratio of 26.21:11.81:53.66:8.32. MP–21 was a neutral polysaccharide (368 kDa) made of Rha,Ara and Gal at a molar ratio of 1:4.84:5.34. Different functional groups of polysaccharides gave different spectra in the range of 400–4000 cm^{-1} measured by Fourier-transform infrared spectroscopy (FTIR) (Table 2). The excitation wavelengths of root polysaccharides included 3427 (MPS-1)/ 3417 (MPS-2)/3406 (MC-1) /3404(MP)/ 3322 cm^{-1} (MP-1) (O–H stretching), 3120 (MPS-2)/2928 (MP-1) 2931(MP) /2927 cm^{-1} (MC-1) (C–H stretching) 1654 (MPS-1)/1651 (MP-

1)1639 (MPS-2)/1637 cm^{-1} (MC-1) (C=O stretching), 1422(MC-1)1416 (MP-1)/1411 (MPS-1)/1257 cm^{-1} (MPS-2) (C=C stretching vibration), 1000–1200 cm^{-1}(MPS-1 and MPS-2) (C–O–H and C– O–C, specific to polysaccharide), 1043 (MC-1)/1038(MP-1)/862 (MPS-2)/860 cm^{-1} (MPS-1) (α–pyranose), 950 (MPS-2)/897cm^{-1} (MC-1) (β– pyranose), and 834 (MP-1)/573 (MC-1) cm^{-1}(α–glycosides) (Wang, Zou et al., 2016; Zhang, Wang et al., 2016; Li, Sun et al., 2017; Tang et al., 2017; Zhang, Zhao et al., 2017). These results should be useful for authenticating maca derived polysaccharides.

2.2.1.3. Dietary fiber

Contents of total dietary fiber, soluble and insoluble dietary fibers of maca roots were 15.6−26.0, 2.6−7.9%, and 14.8−23.4% (dry weight), respectively (Chen et al., 2017; Li et al., 2017). Total dietary fiber content of roots of seven maca samples ranged from 18.3–25.6 %. The contents of soluble and insoluble dietary fibers ranged from 2.6–7.7% and 14.8–22.4%, respectively (Chen et al., 2017). Purple and black maca had higher total and insoluble dietary fiber contents than yellow maca (Chen et al., 2017). Apart from the genetics, influence of cultivation conditions on dietary fiber composition of maca should be considered.

Dietary fibers of maca root were isolated from a liquor residue, using enzymatic or chemical methods (Chen, Zhao et al., 2015). Compared to soybean dietary fiber, the resulting maca dietary fibers had better functional properties in terms of swelling capacity, water holding capacity, oil holding capacity, and inhibition of glucose adsorption (Chen, Zhao et al., 2015). Maca and its byproducts represent a natural source of datary fibers. Techniques remain be developed for incorporating maca dietary fiber to functional food formulations.

2.2.2. Aerial parts

2.2.2.1. Total sugar content

Total sugar content of aerial parts (leaf, stem, and inflorescence) of maca at different growth stages ranged from 1.01 to 2.21% (dry basis). Photosynthesis, respiration, transportation, and distribution of assimilates were major influencing factors (Jin et al., 2018). Types of the sugars derived from the aerial parts remain to be studied.

2.2.2.. Non-starch polysaccharide

A hetero–polysaccharide (MLP–1) (42.756 kDa) and a homo–polysaccharide (MLP–2) (93.541 kDa) were extracted from maca leaves (Kang et al., 2018). MLP–1 was made of ribose (Rib), rhamnose (Rha), arabinose (Ara), xylose (Xyl), mannose (Man), glucose (Glc) and galactose (Gal) with a molar ratio of 0.12:0.32:1.50:0.32:1.03:1.00:0.93. MLP–2 was consisted of glucose. The total carbohydrate contents of MLP–1 and MLP–2 were 94.10% and 90.15%, and their uronic acid contents were 1.51% and 20.62%, respectively (Kang et al., 2018). Another study showed that maca leaf polysaccharides (LMLP) were composed of Gal, Ara, Rha, Glu, and Man with a molar ratio of 5.51:4.05:1.15:0.77:0.01 (Li, Hao et al., 2017). The FTIR spectra of leaf polysaccharides were mainly measured for excitation wavelengths of 3500-3200 cm^{-1} (MLP-1, MLP-2)/3600-3200 cm^{-1} (LMLP) (corresponding to hydroxyl groups stretching vibration), 2928 (MLP-1)/2926 (MLP-2)/ 2933(LMLP) (corresponding to C−H stretching vibration of − CH and $-CH_2$), 1629 (MLP-1)/1619 (MLP-2)/ 1734.99 and 1605.69 cm^{-1} (LMLP)(corresponding to C=O stretching of the carbonyl or acetyl group), 1395 (MLP-1)/1420 cm^{-1} (MLP-2) corresponding to C− O stretching vibration), 1200-1010 (MLP-1, MLP-2) and 1239 and 1020 cm^{-1}(LMLP) (corresponding to C−O−C and C−OH stretching vibrations in the pyranose form), and 868, 573 (MLP-1), 863, 570 (MLP-2) and 535 cm^{-1} (LMLP)(corresponding to α-configuration) (Li, Hao et al., 2017; Kang et al., 2018). These results should be useful for authenticating maca based products.

2.3. Protein

2.3.1. Root

2.3.1.1. Amino acid composition

Maca roots (5 yellow,1 black and 1 purple varieties) contained 875–1255 mg/g protein of total amino acids, and the ratio of essential amino acids to total amino acids ranged from 0.21 to 0.28 (Chen et al., 2017). The contents of total essential amino acids and non–essential amino acids were 189–313 and 634–942 mg/g protein, respectively. The 7 essential amino acids included threonine, valine, methionine phenylalanine, isoleucine, leucine, and lysine with ranges of 24–43, 37–81, 6–57, 24–39, 24–42, 35–51, and 36–61 mg/g protein, respectively (Chen et al., 2017). The 10 non–essential amino acids included aspartate, glutamate, serine, histidine, glycine, arginine, alanine, tyrosine, cysteine and proline in ranges of 54–91, 61–123, 17– 25, 15– 34, 31–44, 76–238, 28–41, 15–21,1–3, and 287–423 mg/g protein, respectively (Chen et al., 2017). Another study showed that valine (65 mg/g protein) was the most abundant essential amino acid in yellow maca root, followed by lysine (50 mg/g protein), leucine (46 mg/g protein), isoleucine (37 mg/g protein), threonine (33 mg/g protein), phenylalanine (32 mg/g protein), and methionine (9 mg/g protein) (Li, Chen et al., 2017). Arginine (202 mg/g protein) was the most abundant non-essential amino acid of the yellow maca root, followed by glutamate (139 mg/g protein), aspartate (83 mg/g protein), glycine (43 mg/g protein), histidine (28 mg/g protein), alanine(39 mg/g protein), serine (25 mg/g protein), tyrosine (23 mg/g protein), cysteine (3 mg/g protein), proline 0.5 (mg/g protein) (Li, Chen et al., 2017). The differences in the amino acid composition from different studies could be due to the differences in maca genetics, cultivation conditions, and analytical methods. It is necessary to evaluate the bioavailability of amino acids from maca proteins and maca protein-containing products.

2.3.1.2. Endogenous enzymes

Endogenous enzymes (amylase, pectin esterase, and polygalacturonase) extracted from commercial maca roots from Peru displayed a maximum activity at pH 6.1 and 33.6°C, pH 6.6 and 49.4 °C, and pH 5.4 and 46 °C, respectively (Rondan–Sanabria, Pires, & Filho, 2006). Maca amylase had a higher optimum pH (6.1) and a lower optimum temperature (33.6°C) of action than that of cassava, ichoimo, Peruvian carrot, sweet potato, and yam (Rondan–Sanabria et al., 2006). Maca pectin esterase showed an optimal pH (6.6) and temperature (49.4 °C) different from that of acerola (pH 9.0, 90°C), apple (pH 6.5, 25°C), banana (pH 7.0, 64°C), carrot (pH 7.4, 48.5°C), grapefruit (pH 7.0, 25°C), green beans (pH 7.5, 25°C), mango (pH 7.0, 30°C), orange (pH 7.5, 60°C), papaya (pH 7.0, 30°C), peach (pH 8.0, 60°C), pear (pH 6.5–7.4, 30°C), Peruvian carrot (pH 6.5 25°C), and potato (pH 7.5, 55°C) (Rondan–Sanabria et al., 2006). Maca root polygalacturonase had higher optimum pH (5.4) and temperature (46 °C) of action than that in some other fruits and vegetables, including banana (pH 3.3–4.3, 37°C), mango (pH 4.5, 37°C), pear (pH 4.7, 30 °C), Peruvian carrot (pH 4.4, 30°C), and tomato (pH 4.5, 37°C) (Rondan-Sanabria et al., 2006). It is necessary to control the enzymatic activity in maca roots, in order to obtain related ingredients of desirable quality (e.g., delayed deterioration after harvest or during food processing).

2.3.2. Aerial part

In aerial parts of maca, the concentrations of 17 amino acids varied among five developing stages (Jin et al., 2018). Total amino acid content ranged from 13 to 24 g/100 g (dry basis). Essential amino acids accounted for 41–47% of the total amino acids. Specifically, the contents of threonine, tyrosine, valine, methionine, isoleucine, leucine, phenylalanine and lysine were at arranges of 0.78−1.41, 0.68−1.15, 0.86−1.55, 0.34−0.49, 0.18−1.33, 1.62−2.11, 0.83−

1.45, and 0.89−2.15 g/100 g (dry basis), respectively (Jin et al., 2018). Non-essential amino acids included aspartic, glutamic, serine, glycine, histidine, arginine, alanine, proline, and cysteine with ranges of 0.83−2.75, 1.27−3.69, 0.75−1.46, 0.88−1.46, 0.36−0.68, 1.09−2.05, 0.83−1.62, 0.93−1.66, and 0.01−0.11 g/100 g (dry basis), respectively (Jin et al., 2018). Overall, the aerial part of maca was seen to be a source of amino acids.

2.4. Lipid

2.4.1 Root

There was a small amount of lipids in maca roots (0.59−2.2%) (Dini et al., 1994; Chen, Xia, Zhu, & Bai, 2015; Guo, Gao, Gu, Wan, Lu., Qin, & Luo, 2016; Li, Chen et al., 2017). The level of unsaturated fatty acids (52.7%) was higher than that of saturated fatty acids (40.1%) (Dini et al., 1994; Li, Chen et al., 2017). The predominant unsaturated fatty acid was linoleic acid (32.6 %), followed by oleic acid (11.1%) (Dini et al., 1994). Among saturated fatty acids, palmitic acid (23.8%) was predominant, followed by stearic acid (6.7%) (Dini et al., 1994).

2.4.2. Aerial part

Maca aerial parts contained essential oils mainly constituted by phenylacetonitrile, benzaldehyde, and 3–methoxyphenylacetonitrile (Tellez, Khan, Kobaisy, Schrader, Dayan, & Osbrink, 2002).

2.5. Mineral

2.5.1. Root

Maca roots contained macrominerals (e.g., calcium, magnesium, sodium, potassium) and trace minerals (e.g., iron, manganese, copper, zinc, cobalt) (Zhang, Wang, Zhao, Zuo, Wang, & Jin, 2015; Chen et al., 2017). Potassium (5394–8063 mg/kg, dry basis) was the most abundant mineral in maca root, followed by calcium, magnesium, sodium, iron, zinc, manganese and

copper in ranges of 5394–8063, 3839–4502, 625–837, 138–188, 58–550, 23–31, 10–17 and 4–8 mg/kg (dry basis), respectively (Chen et al., 2017). Soil minerals at different cultivation areas influenced the mineral composition of maca (Chen et al., 2017). For example, one study showed that the iron concentration of maca root positively correlated with the iron concentration of the soil (Chen et al., 2017). The levels of boron, cobalt, chromium, lithium, nickel and zinc in maca cultivated in China (8.1–21, <0.023, <1.1, 0.02–0.17, 0.085–4.5, and 10–39 mg/kg, dry basis, respectively) differed from those of maca cultivated in Peru (6.6–12, <0.023, <1.1, 0.035–0.063, 0.68–1.7, and 27–39 mg/kg, dry basis, respectively) (Zhang, Wang et al., 2015). The contents of these micronutrients should also depend on the maca genetics.

2.5.2. Aerial part

Depending on growth stages, the levels of potassium, calcium, magnesium, sodium, iron of aerial parts of maca (leaf, stem, and inflorescence) varied between 3588 and 7528, 1339 and 3231, 267 and 543, 19 and 172, and 17 and 84 mg/kg (dry basis), respectively (Jin et al., 2018).

2.6. Vitamin

2.6.1. Aerial part

Vitamin C content in aerial parts of maca ranged from 163 to 236 mg/100 g (dry basis), depending on growth stages and cultivation environments. Niacin content of the aerial parts ranged from 35 to 135 mg per 100 g (dry basis). Both the contents of vitamin C and niacin were considerably higher than those of cabbage and lettuce (Jin et al., 2018).

2.7. Other minor constituents

2.7.1 Root

A variety of minor components with various bioactivities were identified in maca root (Tables 3 and 4). A total of 160 minor compounds (secondary metabolites) were identified in a

methanol extract of maca root. Maca extracts were a source of organic acids, glucosinolates, β–carboline alkaloids, common amide alkaloids, imidazole alkaloids (lepidine A, B, C, and D), pyrrole alkaloids macapyrrolins A, B, and C), macamides (derivatives of 1,2–dihydro–N–hydroxypyridine, benzylated alkamides, macaenes) (Zhou et al., 2017). Among them, glucosinolates (10.97~79.84 mg/g, dry basis) and alkaloids (0.54~2.99 mg/g, dry basis) were the two predominant constituents (Muhammad, Zhao, Dunbar, Khan, 2002; Cui, Zheng, He, & Zheng, 2003; Jin, Chen, Dai, & Yu, 2016; Zhou et al., 2017; Zhou et al., 2018). Another study identified a total of 13 compounds from maca root extracts, including different types of polyphenols such as flavonolignans and phenolic acids (Bai, Kan, Roller, Lai, Bai, & Pan, 2015). Therefore, the minor constituents of maca root is very diverse.

2.7.1.1 Alkaloid

The total content of alkaloids in maca roots depended on cultivation areas and color types, ranging from 0.20 to 2.99 mg/g dry weight (Chen et al., 2017). Maca contained five major alkaloids, namely macamides, common amide alkaloids, macaridines, β–carboline alkaloids, and imidazole alkaloids (Zhou et al., 2017). Purple and black maca were reported to contain more alkaloids than yellow maca (Chen et al., 2017).

2.7.1.2. Macamide

Macamides are secondary amides in maca root, formed from benzylamine and a fatty acid moiety with varying hydrocarbon chain lengths and degree of unsaturation (Muhammad et al., 2002; Ganzer., Zhao, Muhammad, & Khan 2002; Ganzera et al., 2002; McCollom, Villinski, McPhail, Craker, & Gafner 2005; Zhao et al., 2005; Zhou et al., 2017). The contents of macamides ranged from 0.54 to 2.95 mg/g (dry weight) in 17 maca samples. N–benzyl hexadecanamide contents ranged from 0.095 to 0.194 mg/g. One study reported two benzylated

alkamides (macamides) (N–(3,4–dimethoxybenzyl)–hexadecanamide and N–benzyltetracosanamide from a non–polar extract of the root) (Chain, Grau, Martins, & Catalán, 2014). N–benzylhexadecanamide, N–benzyl–(9Z)–octadecenamide, N–benzyl–(9Z, 12Z)–octadecadienamide, N–benzyl–(9Z, 12Z, 15Z)–octadecatrienamide and N–benzyloctadecanamide were also identified by McCollom et al. (2005). The content of macamides in a petroleum ether extract was 20%, among which that of N–benzylpalmitamide, N–benzyloleamide, and N–benzyllinoleamide were 6.63, 4.59, and 4.22%, respectively (Yang et al., 2016).

In an ethanol extract of maca root, six macamides were identified, including N–benzyl–(9Z,12Z,15Z)–octadecatrienamide, N–(3–methoxybenzyl)–(9Z,12Z)–octadecadienamide, N–benzyl–(9Z,12Z)–octadecadienamide, N–(3–methoxybenzyl)–hexadecanamide , N–benzylhexadecanamide , and N–benzyl–(9Z)–octadecenamide (Lin et al., 2018). According to Zhao et al. (2015), maca root contained several alkamides (amide linked with various fatty acids), such as N–benzyl–9–oxo–12Z–octadecenamide , N–benzyl–9–oxo–12Z,15Z–octadecadienamide , N–benzyl–13–oxo–9E,11E–octadecadienamide , N–benzyl–15Z–tetracosenamide, and N–(m–methoxybenzyl) hexadecanamide (Zhao, Muhammad, Dunbar, Mustafa, & Khan, 2005). These compounds had the amine moiety N–benzyl. The acyl chains were unbranched, variable in lengths and unsaturation degrees, and sometimes contained a keto group (Zhao et al., 2005). The alkamides could be used as markers for authentication and standardization of maca products.

The composition of macamides varied with cultivation condition, geographical origin, root color, drying process, and storage period (Pan et al., 2016; Lin et al., 2018). An ethanol extract of black maca (cultivated in China) had the highest total amount of macamides, followed

by white maca (cultivated in China), white maca (cultivated in Peru), and purple maca (cultivated in China) (Lin et al., 2018). N–benzylhexadecanamide and N–benzyl–(9Z, 12Z)–octadecadienamid were dominant in the extracts of maca from Peru and China, respectively (Lin et al., 2018). Black maca root had the most abundant macamides (Pan et al., 2016, Lin et al., 2018). Storage (six month) and drying process (especially steaming) reduced the macamide concentration (Pan et al., 2016).

2.7.1.3. Imidazole alkaloid

A total of 4 imidazole alkaloids were identified in maca root extract, including 1,3–dibenzyl–4,5–dimethylimidazolium chloride (lepidiline A), 1,3–dibenzyl–2,4,5–trimethylimidazolium chloride (lepidiline B) (Cui et al., 2013), 3–benzyl–1–(3–methoxybenzyl)–4, 5–dimethylimidazolium chloride (Lepidiline C), and 3– benzyl–1–(3–methoxybenzyl)–2, 4, 5– trimethylimidazolium chloride (lepidiline D) (Jin, Chen, Dai, & Yu, 2016) (Figure 2).

2.7.1.4. Macapyrrolin

Macapyrrolins (A, B, C) were isolated from 80% aqueous acetone extract of maca roots (Zhou et al., 2018). They were 1–benzyl–5–(methoxymethyl)–1H–pyrrole–2–carbaldehyde (macapyrrolin A), 1–(3–hydroxybenzyl)–5– (methoxymethyl)–1H–pyrrole–2–carbaldehyde, (macapyrrolin B), and 1–(3–hydroxybenzyl)–5–1–benzyl–5–(hydroxymethyl)–1H–pyrrole–2–carbaldehyde (macapyrrolins C). These isolated macapyrrolins (> 40 μM) were toxic to several human cancer cells (Zhou et al, 2018).

2.7.1.5. Macaene

Dried maca root contained 0.09–0.45% of macaenes (acyclic polyunsaturated oxoacids) (Ganzera et al., 2002). A total of 11 macaenes were identified from 17 maca samples (Zhou et

al., 2017). 5–oxo–6E, 8E–octadecadienoic acid was the most abundant macane (Figure 2) (Muhammad et al., 2002; Zhou et al., 2017).

2.7.1.6. Glucosinolate

Maca glucosinolates are anionic sulfur–rich secondary metabolites. Glucosinolates and their hydrolysis products (catalyzed by the endogenous enzyme myrosinase) play roles in plant defense system (Gil & MacLeod, 1980). Approximate 1 % of the fresh weight of maca were glucosinolates, which impart maca the unique pungent flavor. As a comparison, the glucosinolate contents of other cruciferous vegetables were 1.6–2.5% for Brussels sprouts, 0.4–0.8% for cauliflower, 0.4–0.9% for white cabbage, 0.3–10% for red cabbage, 0.6–2.0% for savoy cabbage, and 0.1–0.7% for radish (fresh weight basis) (Rosa, Heaney, Fenwick, & Portas, 1997; Li, Ammermann, & Quirós, 2001; Piacente et al., 2002).

Maca root contained various glucosinolates, such as glucotropaeolin, glucoalyssin, glucobrassicanapin, and glucobrassicin (Dini, Tenore, & Dini, 2002; Li, et al., 2001; Piacente et al., 2002; Wang, Wang et al., 2007; Yabar et al., 2011). Three different maca ecotypes (yellow, red and black) from Peru had similar glucosinolate composition (Yábar, Pedreschi, Chirinos, & Campos, 2011). Six glucosinolates identified in the maca roots (yellow, red and black) included three aromatic compounds: 4–hydroxybenzyl (glucosinalbin), benzyl (glucotropaeolin) and 3–methoxybenzyl (glucolimnanthin); one aliphatic compounds: 5–methylsulfinylpentyl (glucoalyssin) and two indolic compounds: 4–hydroxy–3–indolylmethyl (4–hydroxyglucobrassicin) and 4–methoxy–3–indolylmethyl (4–methoxyglucobrassicin) (Table 1). Among them, 80–90 % of the total maca glucosinolates were composed of glucotropaeolin (benzyl glucosinolate) (Clement et al., 2009; Yábar et al., 2011). Chen et al. (2017) found that the content of benzyl glucosinolate (0.28–1.64 mg/g) varied in 7 different maca roots.

The composition of glucosinolates in maca depended on the developmental stage, plant parts, cultivation practices (i.e., climatic conditions), ecotype (i.e., colors), pre–and post–harvest handling (i.e., length of boiling time), and product types (Li et al., 2001; Dini, et al., 2002; Piacente, Carbone, Plaza, Zampelli, & Pizza; 2002; Gonzales et al., 2005; 2007; Clement et al., 2010; Yábar, Pedreschi, Chirinos, & Campos, 2011). Fresh roots had the highest total glucosinolate content, followed by seeds, sprouts, dried root, and fresh leaves (Li et al., 2001). Red maca aqueous extract had a higher glucosinolate content than extracts from black and yellow ecotypes (Gonzales et al., 2005). The glucosinolate content of spray-dried hydroalcoholic extract of red maca from 2-hour boiling was higher than that from 3-hour boiling (Gonzales et al., 2007). A higher total glucosinolate content was found in maca root at 15–30 days after harvesting than that of roots at harvest and roots at 15 days before harvesting time (Yábar et al., 2011). Positive correlation between the total glucosinolate content and myrosinase activity was observed (Yábar et al., 2011). Post-harvest processing remained to be optimized to maximize the content of maca glucosinolates for human nutrition.

2.7.1.7. Polyphenol

Phenolic composition of maca were influenced by the ecotypes such as the color (Korkmaz, 2018). Total phenolic contents of black, yellow and red maca freeze-dried extracts were comparable (~0.57 g of pyrogallol/100g) (Gasco et al., 2008). The total phenolic content in a hydroalcoholic extract of black maca was 0.65 g pyrogallol/100 g (Rubio, Yucra, Gasco, & Gonzales, 2011). Hydroalcoholic extract of black maca had a higher total phenolic content (1.35 g gallic acid/100 g extract) than hydroalcoholic extract of red maca (1.16 g gallic acid/100 g extract) (Zevallos-Concha, Nuñez, Gasco, Vasquez, Quispe, & Gonzales, 2016). Total phenolic contents in red and black maca increased after γ-irradiation processing (8 kGy) by 17 and 33%,

respectively (Zevallos-Concha et al., 2016). γ-Irradiation possibly improved the extractability of the phenolics.

Quercetin (Lee et al., 2004) and anthocyanins (Valerio & Gonzales, 2005) were found in maca root. Maca root is a source of flavonolignans, such as tricin 4′-O-[threo-β-guaiacyl-(7″-O-methyl)-glyceryl] ether, and tricin 4′-O-(erythro-β-guaiacyl-glyceryl) ether (Figure 2).

2.7.1.8. Phytosterol

Maca roots contained a mixture of steryl acetate derivatives, including sitosteryl acetate, campesteryl acetate, ergosteryl acetate, brassicasteryl acetate and $\Delta^{7,22}$–ergostadienyl acetate at a concentration percentage ratio of 45.5: 27.3: 13.6: 9.1: 4.5 (Table 1) (Dini et al., 1994).

2.7.1.9 Volatile compound

In fresh maca root, a total of 14 volatiles was identified using thermal-desorption cryo-trapping-gas chromatography-mass spectrometry (TCT-GC/MS). The most abundant was isothiocyanates (e.g., 4-ethylphenyl isothiocyanate) (27.26%), followed by chloro-compounds (near 20%), and tetrahydro-3-methylfuran (14%) (Zheng et al., 2013).

2.7.2 Aerial part

At different growth stage, aerial part (leaf, stem, and inflorescence) of maca contained glucosinolates, macamides and saponins at ranges of 31.4–36.2, 0.451−0.703, and 33.2−51.8, mg/g (dry basis), respectively (Jin et al., 2018). In fresh maca leaves, a total of 14 main volatiles were identified. Acetic acid (17.1%), cyclopentane (12.4%), and 3, 3-dimethylglutaric anhydride (12.0%) were the most abundant (Zhang et al., 2013).

In another study, a total of 22 phenolics (93.5%), including 2 nitrogen (85.9%), 14 oxygen (4.5%), 1 sulfur (0.4%), 1 nitrogen and oxygen (2.1%), and 2 nitrogen and sulfur (0.6%)

substituted phenolics, were among 53 compounds identified in the essential oil of maca aerial parts (Tellez et al., 2002). However, the exact types of these phenolics remain to be identified.

3. Biological activities

Maca has been demonstrated to possess multiple biological properties, such as improving reproductive health (Table 3), antifatigue, antioxidative, neuroprotective, hepatoprotective, antiviral, antimicrobial, anticancer, and immune–regulatory capacities (Table 4).

3.1. Effects on the male and female reproductive systems

Maca consumption has been traditionally associated with its positive effects on human reproduction health, namely enhancing sexual libido, fertility, and spermatogenesis (Balick & Lee, 2002; Beharry & Heinrich, 2018). The observed effects mainly depended on the sensitivity of selected experimental model systems (e.g., animal types, physiological biomarkers, study length) to maca extract or powder (Beharry & Heinrich, 2018). Readers are encouraged to refer to the most recent review article of Beharry and Heinrich (2018), who summarized the current understanding on maca effects on the reproductive health of animals and humans. Indicators of reproductive functions in males were sexual desire and several features of human semen (e.g., some physical characteristics of the ejaculate, sperm number, sperm motility, and various aspects of sperm function). Menopausal symptoms and hormone levels were used as indicators of reproductive function in females. Scientific understanding is still unavailable in terms of (1) principle active components of maca responsible for the observed physiological beneficial effects (only few components were tentatively proposed) (Table 4), (2) mechanism of action involved in those positive physiological responses *in vivo*; 3) optimization of *in vivo* evaluation systems (Beharry & Heinrich, 2018).

3.1.1. Beneficial effects on male reproductive systems

Beneficial effects of maca powder or extract administration on spermatogenesis were observed in various male animal models, including Holtzman male rats (the mostly used rodent model), Ansell male mice, peri–pubertal breeding bulls, BALB/c male mice, Swiss strain mice, and male Saint Croix rams (Aslam et al., 1999; Gonzales et al., 2001b; 2003b; 2004; 2006a, 2006b; Chung et al., 2005; Gasco et al., 2007a Ray et al., 2015). Secondary metabolites such as phenolics were possible spermatogenesis promoters (Inoue, Farfan, & Gonzales, 2016; Yucra et al., 2008). Black (and yellow, to a lesser extent) maca extract more triggered certain spermatogenesis related biomarkers than red maca (Gonzales et al., 2006a; Gasco et al., 2007; Inoue et al., 2016). Several physiological biomarkers were sensitive to maca treatment conditions, including frequency and length of stage VIII of spermatogenesis, daily sperm production, sperm count in the vas deferens, and epididymal sperm count (Beharry, & Heinrich, 2018).

Some studies showed that maca root aqueous extracts protected male spermatogenesis against external environmental stress, such as high altitude exposure, malathion or lead acetate induced damages (Gonzales et al., 2004; Bustos–Obregon et al., 2005; Rubio et al.; 2006). Other studies reported preventative effects of red maca aqueous and hydro–alcoholic extracts in testosterone enanthate induced prostatic hyperplasia (Gonzales et al.2005; 2006a; 2007; 2008; 2012; Noratto et al.; 2013). Glucosinolates and their metabolites (benzyl glucosinolate, in particular) in red maca extracts possibly contributed to the preventative effects via regulating stromal cells and zinc level (Gonzales et al.2005; 2006a; 2007; 2008; 2012).

Maca improved male sexual performances of mice and rats with hypogonadism, Sprague–Dawley rats, male Sanit Coix rams, Kunming mice, and diabetic male rats (Zheng et

al.., 2000; Cicero et al., 2001; 2002; Lentz, Gravitt, Carson, Marson, & Giuliano, 2007 ; Lavana, Vazquez, Palma–Irizarry, & Orihuela, 2013; Kimura, Horie, Yamaguchi, Muto, Ide, & Abdelhamed, 2016; Zhang, Yu, Jin, & Ao, 2016; Avelar et al., 2016). These animals fed with maca samples showed improvements in erectile dysfunction, post–ejaculatory latency, mount latency, number of ejaculations, premature ejaculation, and libido (Zheng et al., 2000; Cicero et al., 2001; 2002; Lentz et al., 2007; Kimura et al.; 2016; Lavana et al., 2013; Zhang, Yu et al., 2016). Possible bioactive components involved included polysaccharides, macaenes, macamides, benzyl isothiocyanate, *p*–methoxy benzyl isothiocyanate, non–polar alkaloids, and aromatic isthiocyanates (Zheng et al., 2000; Cicero et al., 2001; 2002; Zhang, Yu et al.; 2016).

According to clinical trials, maca samples (gelatinized powder, pills, pulverized and dehydrated capsule, dried milled hypocotyl) improved several features of human semen (e.g., ejaculation volume and total sperm count) of healthy males and males with sub–subfertility (Gonzales et al., 2001a; Tancara et al., 2010; Tancara et al., 2010; Melnikovova, Tomas, Huml, Kolarova, Lapcik, & Cusimamani, 2014; Melnikovova, Fait, Kolarova, Fernandez, Milella, & Kim, 2015). Maca (tablets containing pulverized and/or dehydrated roots, capsule) improved sexual desire and well–being performance of healthy males and males with dypogonadism or mild erectile dysfuntion (Gonzales et al., 2002; Poyato, Torres, & Rita, 2009; Stone, Ibarra, Roller, Zangara, & Stevenson, 2009; Zenico, Cicero, Valmorri, Mercuriali, & Bercovich, 2009). Melnikovova et al. (2015) considered macamides as a major type of the active compounds responsible for these effects.

3.1.2. Beneficial effects on female reproductive systems

According to animal trials, maca powder or extracts improved female fertility in ICR mice (not sexually mature), Sprague–Dawley female rats, and female breeder rats (Table 3)

(Oshima, Gu, & Tsukada, 2003; Ruiz–Luna, Salazar, Aspajo, Rubio, Gasco, & Gonzales, 2005; Meissner, Kedzia, Mrozikiewicz, & Mscisz, 2006a; Pino-Figueroa & Maher, 2009; Uchiyama Jikyo, Takeda, & Ogata, 2014). Maca powder or extract also effectively alleviated certain menopausal symptoms of various rats/mice, such as Wistar female sexually experienced rats (ovariectomized and sham–operated), ovariectomised rats, Sprague–Dawley rats, Swiss type female mice (Ruiz-Luna et al., 2005; Meissner et al., 2006a; Zhang, Yu, Ao, & Jin, 2006; Zhang, Yu, & Ao, 2008; Zhang, Yu, Jin, & Ao, 2014; Wang, Yang, Wang, & Bian, 2009; Gonzales et al., 2010; Barraza et al., 2015). In addition to the animal type, factors influencing the efficiency included maca format (powder *vs* extract, black *vs* red *vs* yellow maca), dosage, and study duration, which possibly determined the key active compounds, toxicity, and short–term and long–term effects, respectively (Beharry & Heinrich, 2018).

Based on clinical trials on healthy early–menopausal, or menopausal, or postmenopausal women, maca powder and extracts promoted sexual functions of the female reproductive systems (Table 3). The improvements were related to alleviated menopausal symptoms, balanced hormone, increased bone density, improved orgasm (post–menopausel women only), and anti–depression effects (Meissner, Kapczynski, Mscisz, & Lutomski, 2005; Meissner et al., 2006c; 2006d; Meissner, Reich-Bilinska, Mscisz, & Kedzia, 2006e; Brooks, Wilcox, Walker, Ashton, Cox, & Stojanovska, 2008; Stojanovska, Law, Lai, Nelson, Chung, & Haines, 2011; Dording et al., 2015).

In contrast to the above mentioned positive effects, some studies showed that maca extracts or powder had no effects on the function of reproductive systems *in vivo.* In animal trials, for example, red, yellow and black maca aqueous lyophilized extracts did not influence the reproductive parameters in Holtzman female rats (Gasco et al., 2008). Milled maca dried roots

and yellow maca aqueous extracts did not affect the semen parameters in male rats and rams (Chung et al., 2005; Lavana et al., 2013). In clinical trials, maca capsule consumption did not positively alter the biomarkers involved in depression, sexual quality or overall well–being of postmenopausal women (Stojanovska et al., 2015). Fertility enhancing property of maca in male and female, therefore, is considered to be inconclusive and deserves further evaluation (Beharry & Heinrich, 2018).

3.2. Antifatigue

The antifatigue effect of maca was evaluated by the forced swimming test using different mice models, including male Kunming mice and ICR mice (males and females) (Li et al., 2017, Tang et al., 2017). Mice swimming performance (average swimming speed and prolonged swimming duration) and related biochemical parameters were indicators. Using the swimming test, the antifatigue activity were determined on several biomarkers, such as glutathione peroxidase, lactate dehydrogenase, creatine kinase, blood urea nitrogen, malondialdehyde, lactic acid, blood lactate, and liver glycogen. Dried yellow maca root powder (Li, Chen et al., 2017), macamides (Yang et al., 2016), polypeptides (Miao et al., 2015), and polysaccharides (Li, Sun et al., 2017; Tang et al., 2017) could be used for antifatigue purpose. Li et al. (2017) showed that maca root powder at a dose of 400 mg/kg bw/d for 30 days prolonged swimming duration, increased liver glycogen content, and decreased blood lactic acid of male Kunming mice. Tang et al. (2017) demonstrated that maca polysaccharides, at the most effective dose of 100 mg/kg for 30 days, accelerated the average swimming speed and prolonged the swimming time of male and female ICR mice. The polysaccharides effectively enhanced the activities of serum antioxidants (glutathione peroxidase and creatine kinase lactate dehydrogenase), while reducing metabolic products (blood urea nitrogen, lactic acid, and malondialdehyde). In this case, 100 mg/kg

polysaccharides were equivalent to daily recommended dosage of 14 g maca powder for humans (Tang et al., 2017). Li, Sun et al. (2017) reported that a maca root polysaccharide fraction (MPS–2) had a better antifatique effect than the polysaccharide fraction (MPS–1). This difference could be due to the differences in monosaccharide composition and molecular weight between MPS–1 and MPS–2. According to Yang et al. (2016), N–benzyloleamide (40 mg/kg), followed by N–benzyllinoleamide (40 mg/kg), were effective antifatigue bioactives in swimming Balb/c mice. Mao et al. (2015) reported that maca polypeptides improved fatigue related physiological indexes of healthy mice, including blood glucose, urea nitrogen, and creatinine (Mao et al., 2015). Relationships between the structure of maca polysaccharides and antifatigue property have not been fully characterized. The antifatigue effect of maca remains to be evaluated using human clinical trials. Although these *in vivo* trials revealed the antifatigue potential of maca, existing antifatigue drugs should be used for comparison. In addition, mechanism of action is worthy investigating to provide scientific evidence for developing maca as a potential natural antifatigue agent.

3.3. Antioxidation

Maca root polysaccharide (1067 kDa) and leaf polysaccharide fractions (42.8, 58.4, and 93.5 kDa) had different levels of *in vitro* scavenging capacities on hydroxyl, DPPH, and superoxide anion radicals (Zhang et al., 2017; Kang et al., 2018; Li, Hao et al., 2017). FRAP values of root polysaccharide (1067.3 kDa) and leaf polysaccharide (58.43 kDa) fractions were dose–dependent (Zhang et al., 2017; Li, Hao et al., 2017). A leaf polysaccharide fraction (MLP–1) had a higher radical scavenging ability than another polysaccharide fraction (MLP–2), possibly due to its lower molecular weight (lower viscosity of sample solution), and more complex monosaccharide composition (additive or synergetic effects on hydroxyl radical

scavenging) (Kang et al., 2018). *In vivo*, polysaccharides from water extract of oven–dried maca roots and macamides (N–benzyl–oleamide (most effective), N–benzyl–linole–amide) positively altered the antioxidant status of ICR mice during forced swimming tests (Tang et al., 2017) and Balb/c mice (Yang et al., 2016), respectively. Antioxidants of maca include polyphenols, glucosinolates, alkamides, and polysaccharides (Korkmaz, 2018).

3.4. Neuroprotection

The neuroprotective property of a pentane extract of maca root was demonstrated *in vitro* using crayfish neurons with H_2O_2 induced oxidative stress (effective concentration 50% (EC_{50}): 2.8 µg/mL), and *in vivo* using male Sprague–Dawley rats in stroke conditions (effective dose of 3 mg/kg) (Pino–Figueroa, Nguyen, & Maher, 2010). Using 1–methyl–4–phenyl–1, 2, 3, 6–tetrahydropyridine (MPTP)–induced zebrafish model, the neuroprotective effects of a fraction of methanol extracts of maca and macamides were observed (Zhou et al., 2017). Male ICR mice fed with maca powder for 5 weeks had improved mitochondrial activity and modulation of autophagy signaling in the cortex (Guo et al., 2016). Mice treated with an ethanol (EtOH) extract of black maca for 4 weeks dose–dependently showed increased cognitive performance during memory tasks (especially those related to improved spatial learning and memory). Ovariectomized mice fed with an aqueous extract of dried black maca root for 7 days had increased step–down latency,learning, and memory. Kunming strain male mice fed with both queous and hydroalcoholic extracts of black maca roots for 35 days exhibited improved dscopolamine–induced memory and learning impairment (Rubio, Dang, Gong, Liu, Chen, & Gonzales, 2007).

Possible neuroprotective components of maca included alkaloids, benzylated amides (macamides), polyunsaturated oxoacids (macaenes), benzylisothiocyanates, N–3–

methoxybenzyl–linoleamide, and polyphenols (Pino–Figueroa et al., 2010, Rubio, Yucra et al., 2011; Almukadi et al., 2013). For example, polyphenols (i.e., quercetin and anthocyanins) in black maca enhanced the cognitive performance of rats (Rubio, Yucra et al., 2011; Rubio, Qiong, et al., 2011). The inhibition of acetylcholinesterase (AChE), butyrylcholinesterase (BuChE), or fatty acid amide hydrolase (FAAH), modulating the release of neurotransmitters, antioxidative, or antiapoptotic effects were the possible mechanisms behind neuroprotective effect of the maca samples (Pino-Figueroa, Nguyen, & Maher, 2010; Rubio et al., 2007; Rubio, Qiong, et al., 2011; Rubio, Yucra et al., 2011; Almukadi et al., 2013; Guo et al., 2016; Zhuo et al., 2017).

3.5. Anticancer

In vitro, macapyrrolins A, B and C (Figure 2) (> 40 μM) were antiproliferative against NB4 (human acute promyelocytic leukemia cell line), A549 (human lung adenocarcinoma epithelial cell line), SHSY5Y (human neuroblastoma cell line), PC3 (human prostate cancer cell line), and MCF7 (human breast adenocarcinomacell line) tumor cells (Zhou et al., 2018). Glucosinolates and its digestive metabolites and anthocyanins in aqueous extract of red maca possibly contributed to the anticancer potential against LNCaP prostate cancer cells by increasing mRNA expression of the androgen receptor (AR) and prostate–specific antigen (PSA). The AR plays a critical role in the proliferation of prostate cancer cells. The PSA is a tumor marker for prostate cancer (Díaz et al. 2016). In a previous study, lepidiline B was antiproliferative against the UMUC3, PACA2, MDA231, and FDIGROV cell lines with an effective dose $(ED)_{50}$ of 6.47, 1.38, 1.66, and 5.26 μg/mL, respectively (piacente et al., 2002). The EC_{50} is the concentration that gives half-maximal response. Tricin 4′-O-[threo-β-guaiacyl-(7″-O-methyl)-glyceryl] ether, tricin and lepidiline B were anitiperliferative against HL-60 cells with IC_{50} values of 40.4, 52.0, and 52.1 μM, respectively (Bai et al., 2015). IC_{50} is the

concentration of an inhibitor where the response is reduced by half. Maca flavonoids can also be considered as a potential chemopreventive agent against cancers in humans (Lao et al., 2015).

3.6. Hepatoprotection

In vitro, maca root polysaccharide (MP–1, 1067.3 kDa) dose–dependently protected alcohol induced damage of Hep–G2 cells. *In vivo*, MP–1 had hepatoprotective activity against alcohol induced hepatic injure in mice (Zhan, Zhao et al., 2017). A root polysaccharide fraction (MP–1) was antioxidative *in vitro*, playing a partial role in the hepatoprotective effect of maca in cell models and animal trials (Zhang, Zhao et al., 2017). MP-1 at doses of 200, 600, and 1800 mg/kg alleviated the hepatic injury by positively altering biochemical indicators of the mice treated with alcohol. The changes included lowering alcohol induced elevation in serum activities of alanine aminotransferase, aspartate aminotransferase, gamma glutamyl transferase, inhibiting alcohol-induced increases of the serum total triglycerides (TG) and low-density lipoprotein cholesterol as well as liver malondialdehyde and TG levels, and increasing the levels of liver antioxidant enzymes (superoxide dismutase, glutathione peroxidase, and glutathione s-transferase) (Zhang, Zhao et al., 2017). Histopathologic analysis of liver tissues showed that MP-1 lightened alcohol induced inflammation of mice (Zhang, Zhao et al., 2017). These effects of MP-1 were not in a dose-dependent manner as an excessive amount of MP-1 increased the metabolism burden in liver (Zhang, Zhao et al., 2017). However, *in vitro*, MP-1 (0.125 to 2.0 mg/mL) concentration-dependently lessened alcohol induced damage of Hep-G2 cells. Results from these animal and cell-line models should be further confirmed using biologically relevant human trials.

3.7. Antimicrobial and pesticidal activity

A methanol extract of maca root powder (10–80 μg/mL) showed *in vitro* inhibitory activity against human influenza Type A (Flu–A) and Type B (Flu–B) viruses in infected Madin–Darby canine kidney (MDCK) cells (del Valle Mendoza, Pumarola, Gonzales, & del Valle, 2014). The extract had cytotoxicity against normal MDCK cells with a CC_{50} (the concentration of 50% cytotoxicity) of 850 μg/mL. In MDCK infected cells, the extract inhibited the growth of Flu–A and Flu–B with an IC_{50} (the concentration of 50% inhibition) of 5.4 and 7.69 μg/ml, respectively. Effective compounds in maca root powder against human influenza are still unidentified (del Valle Mendoza et al., 2014).

Maca leaf essential oils have potential as a natural pesticide (controlled destructive pests *Coptotermes formosanus*) (Tellez et al., 2002). 3-Methoxyphenylacetonitrile and benzylthiocyanate derived from maca leaf essential oils represented key bioactive components, which could be an alternative to chemical pesticides (Tellez et al., 2002).

3.8. Immune-regulation

In vitro, maca leaf (LMPL 58.43 kDa) and root (MC–1, 11.3kDA) polysaccharide fractions had immune-regulatory activity on RAW264.7 cells with unclear mechanisms (Li, Hao et al., 2017). LMPL (10–160 μg/mL) stimulated the proliferation of RAW264.7 cells and increased the phagocytosis. Phagocytosis is one of the main processes of the immune response and plays an important role in immune surveillance (Sun, Hu, & Li, 2017).

A polysaccharide fraction (MC–1, 11.3kDa) from maca root contained Man, Glu, and glycosidic bonds of α–(1 → 3)–Man, α–(1 → 4)–Glc, α–(1 → 6)–Glc. MC–1 at below 1000 μg/mL was nontoxic to RAW264.7 cells. MC–1 (at 62.5, 250, and 1000 μg/mL) enhanced the pinocytic and phagocytic capacity to *Escherichia coli* (FITC–labeled) of the cells. At molecular level, MC–1 promoted the release of NO and cytokines (IL–6, IL–10 and TNF–α) by targeting

toll–like receptor 2, complement receptor 3, and mannose receptor (Zhang, Wang et al., 2016). Mechanisms behind immune–regulatory potential of maca polysaccharides are to be better studied.

3.9. Prevention against ultraviolet (UV) radiation

Maca root extract (0.13 mg/mL) was applied on the dorsal surface of male Holtzman rats exposed to short-wavelength ultraviolet (UV-C) radiation for 3 weeks. The extract showed UV blocking activity. Boiling extraction enhanced the preventive effect of the extract. Benzyl glucosinolates and polyphenols were suggested to be responsible for the UV protective effect (Gonzales-Castaneda & Gonzales, 2008).

3.10. Promoting digestion

Male and female Kunming mice with atropine-induced gastrointestinal motility disorder were gavage-fed with powdered aerial parts of maca (at daily doses of 0.54, 1.08 and 2.16 g/kg body weight) for 7 days (Jin et al., 2018). The powder promoted gastric emptying and intestinal propulsion at serum motilin and gastrin level (Jin et al., 2018). Mechanism responsible for the effect of treating gastrointestinal motility disorder has not been elucidated. Benzyl isothiocyanate was thought to be a potential bioactive associated with this effect (Jin et al., 2018).

3.11. Safety of maca products

Maca is one of the traditional herbal medicines in the regions of Peruvian highlands. The substantial historical use of maca is considered as an indirect clinical trial for centuries. Noticeably, traditional herbal medicine implies a combination of diet and herbal remedies as well as mind and spirit in the prevention and treatment of diseases (Singh, Sharma, Chauhan, & Kaur, 2014).

Maca has shown a low degree of acute oral toxicity in animals and cellular toxicity *in vitro* (Valerio & Gonzales, 2005). Maca-induced liver injury was observed in a man (30 year old) after drinking 300 mL of maca based medicinal liquor containing 50% (V/V) alcohol on one occasion 10 days ago. Mechanism of maca-induced liver injury remains to be established (Xiao, He, Chen, & Ma, 2017). In another study, volunteers consumed maca dried root powder (0.6 g/ day) for 90 days and showed moderately increased plasma aminotransferase level and diastolic blood pressure (Valentova et al., 2008). However, this alteration can be eliminated by consuming a mixture of silymarin (seeds of milk thistle) and maca (0.6 + 0.2 g/day) (Valentova et al., 2008). Therefore, maca can be consumed as a food supplement in combination with other components to minimize the adverse effects.

Possible adverse effects and toxicity of maca based products should be further investigated. Most of the studies using animal models did not report toxicity. Results of *in vitro* and animal studies should be translated into useful data through clinical trials. Potential mechanisms of action related to toxicity of maca products should be analyzed to support the translation.

4. Innovation and diversification of maca for food and non-food utilization

4.1. Food uses

Maca root can be baked or eaten after decoction or drying (Toledo et al., 1998). Representatives of commercially available maca products are flour (dried and milled), gelatinized flour (dried, extruded and milled), plain or encapsulated and hydroalcoholic extracts. Areal aerial parts of maca such as leaves could be edible vegetables (Jin et al., 2018). Maca based products remain to be developed for innovation and diversification. The innovation should not modify the sensory profile of maca products for commercial applications.

Product diversification provides opportunities to maximize nutritional and functional potential of maca. Maca ingredients can be introduced into food products to carry out specific technologic functions (e.g., coloring, flavoring, texturizing, antioxidation and preservation). Maca contains various bioactive compounds such as dietary fibers, which can fortify food products such as cereals or baking products for enhanced nutritional quality. Root pigments could be natural food coloring additives. Maca non-starch polysaccharides and starch are possible products from fractionation processing. They can be used as emulsifiers, stabilizers and thickeners to give foods desired texture and consistency. For example, the relatively high viscosity of starch from yellow maca root may be valuable in some areas of the food industry, especially where high thickening power is preferred. The low viscosity of starch from purple maca root may be useful in the paper–making industry, where lower viscosity is desired. The gelation capacity of starch from black maca root may be exploited as a jellifying agent in refrigerated foods (Zhang et al., 2017). Bioactive compounds from maca root and leaves as ingredients can be utilized for manufacturing functional food products. Maca derived antioxidants could be used for preventing lipid-rich foods from developing rancidity and off–flavor, or in control of enzymatic browning of fresh produce. Further research remains to focus on the isolation and fractionation of these active compounds. In addition, appropriate labelling of food products containing maca ingredients remains to be developed.

4.2. Non-food uses

In medicinal practices, maca could be natural phytotherapeutic agents. Maca extracts showed a range of pharmacological effects in animals and humans (Table 4). Quantification of the compounds in maca extracts responsible for the bioactivities should be better done. For medicinal uses, isolated bioactive compounds from maca remains to be systematically evaluated

for their pharmacological mechanisms and toxicity. The isolation and synthesis of the bioactive compounds found in the extracts may lead to the development of maca as a source of phytotherapeutic agents. For example, macamide N–3–methoxybenzyl–linoleamide isolated from maca lipophilic extracts was a fatty acid amide hydrolase (FAAH) inhibitor (Almukadi et al., 2013), which could act as a neuroprotective agent. Considering the antifatique activity found for macamides, further studies should aim at the possible applications of macamides–derived products as antifatigue agents. Bioactive components in underutilized parts of maca such as leaves could be explored as agents for the application in complementary medicine.

In agricultural practices, essential oils of maca aerial parts could be a natural pesticide. 3–Methoxyphenylacetonitrile and benzylthiocyanate identified from maca essential oils were bioactive against the Formosan subterranean termite (*Coptotermes formosanus*), which is currently one of the most destructive pests in the United States (Tellez et al., 2002). Maca essential oils as an alternative to chemical pesticides deserve further studies.

In cosmetics, maca root products prevented UV-A, -B, and –C induced skin damage in rats (Gonzales- Castañeda, & Gonzales, 2008). Maca root could be a UV filtering ingredient for sunscreen or other cosmetic products.

In pet feed industry, maca derived product could be potential therapeutic agents for certain function such as antifatigue, hepatoprotection, neuroprotection, and intestinal motility promotion, having been proved using animal models (Pino-Figueroa et al., 2013; Guo et al., 2016; Tang et al., 2017; Zhang, Zhao et al., 2017; Jin et al., 2018).

5. Comparative studies

Many previous studies made efforts to profile the chemical and biological properties of maca plant without the uses of appropriate standard or control group (i.e., well-studied dietary

plants). A few comparative studies focused on maca samples from different cultivation areas (i.e., Peru vs China), or color types (i.e., yellow vs black maca) (Chen et al., 2017). Less attentions were given to compare the chemical and biological differences among different parts of maca plants (i.e., root vs. stem). A few comparative studies have been done in the chemical composition or physiochemical properties of particular chemical components (i.e, carbohydrate or protein). Such comparative studies described the differences between mara root starch and starches derived from common starchy foods (i.e., potato, maize, and cassava) (Dini et al., 1994; Zhang, Li, et al., 2017), maca dietary fiber and soybean dietary fiber (Chen, Zhao et al., 2015), maca amylase and amylases from cassava, ichoimo, Peruvian carrot, sweet potato, and yam (Rondan-Sanabria et al., 2006). In addition, limited comparison studies evaluated the similarities and differences in chemical profiles (e.g., concentrations and types) between maca plant and other *Brassica* species commonly used in human diet. For example, the contents of vitamin C and niacin were compared in the aerial parts of maca,cabbage, and lettuce (Jin et al., 2018). The glucosinolate contents were compared between maca and other cruciferous vegetables (Brussels sprout, cauliflower, white cabbage, red cabbage, savoy cabbage, and radish (Rosa, Heaney, Fenwick, & Portas, 1997; Li, Ammermann, & Quirós, 2001; Piacente et al., 2002). These comparative studies provide basis to explain the unique nutritional value and physiological effects of maca plant different from those of other dietary plants as described in the sections 2 and 3 above.

It should be stressed that, only under the same experimental conditions and instrumental settings, the results between maca and other plants can be meaningfully compared. Different studies tended to use different experimental and instrumental conditions, making the comparisons in chemical and biological properties between maca and other plants impossible.

For example, **p**harmacological properties of maca in y were of great interests. However, it is difficult to compare the results of different tests in different groups over time. Without a commonly used standard or widely recognized control, results should be interpreted with a caution. The doses employed in different studies remain to be biologically or physiologically relevant. The connections between pharmacological attributes and chemical composition of the maca-derived formulations are lacking. The composition of maca extracts used in the studies were rarely reported. This seriously hinders our understanding in the component-function relationships of maca components. As a result, there is no recommended dietary allowances (RDAs) of maca to meet the known physiological needs of practically healthy persons. RDAs are valuable for industrial new product development and for the guideline establishment of food nutrition labeling.

6. Conclusions and future research

The starchy roots of maca are the edible part traditionally used for proposed fertility-enhancing and other medicinal/nutritional properties. Secondary metabolites found in maca extracts are important bioactive components. Dietary fibers, minerals, non-starch polysaccharides, polyphenols, macaenes, macamides, glucosinolates, and alkaloids are the major biological active compounds in maca. Cultivation conditions, color type, plant parts, and extraction conditions affected the composition of bioactive components in maca extracts. *In vitro* and *in vivo* studies revealed various bioactivities of maca products, such as reproductive promoting, antifatigue, neuroprotective, anticancer, hepatoprotective, and immunomodulatory capacities. Tentatively, protein,some amino acids (e.g., valine, isoleucine), polypeptides, N-

benzyl-oleamide, N-benzyl-linoleamide, polysaccharides (i.e., D-GalA-based, 7.6 and 6.7 kDa) contributed to anti-fatigue property of maca. Root polysaccharide (1067.3 kDa) and leaf polysaccharide fractions (42.8, 58.43 and 93.5 kDa) also contributed its anti-oxidative property. Macamides, alkaloids, benzylated amides (macamides), poly-unsaturated oxoacids (macaenes), benzyl-isothio-cyanates, polyphenolic compounds (i.e., quercetin, anthocyanins contributed to neuro-protective potential of maca. Roots polysaccharide fraction (1067.3 kDa), and both flavonolignan tricin 4′-O-[threo-β-guaiacyl-(7″-O-methyl)-glyceryl] ether and lepidiline B contributed to the hepato-protective and anti-inflammation properties, respectively. Glucosinolates and its digestive metabolites, anthocyanins, flavonolignan tricin 4′-O-[threo-β-guaiacyl-(7″-O-methyl)-glyceryl] ether, tricin and lepidiline B contributed to anticancer properties of maca. Root polysaccharide fraction (11.3 kDa) and leaf polysaccharide fraction (58.43 kDa) are potential immune-regulatory bioactives. Benzyl glucosinolates and polyphenols and benzyl isothiocyanate showed preventive effects against ultraviolet (UV) radiation and gastro-intestinal motility promotion of maca. It should be stressed that many bioactive components have multiple bio-functions. These tentatively assigned biological activities from specific maca components may result from other components and possible synergistic effects. Laboratory and clinical studies showed that maca positively affected sexual functions of the male or female reproductive systems. The reported biological activities were mostly associated with maca extracts without known mechanism and key responsible active components.

There are a number of limitations in above reviewed research that from our current findings and knowledge about maca plant. We would benefit from further research to develop solutions for the following research problems. (1) comparative studies to evaluate similarities and differences in chemical profiling (e.g., concentrations and types) and biological activities

between maca plant and other plants widely used in human diet, especially the *Brassica* species; (2) relationships between the chemical structure and biological activity of maca components; (3) optimized clinical models to prove a relationship between maca functional components and the claimed health effects; (4) specific health–promoting roles of maca derived functional components in different stages of disease control; 4) toxicological property of maca as a phyto-therapeutic agent; (5) diversifying maca based products for food and industrial applications; (6) characterize and use underutilized parts of maca such as leaf.

Declaration

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Declaration

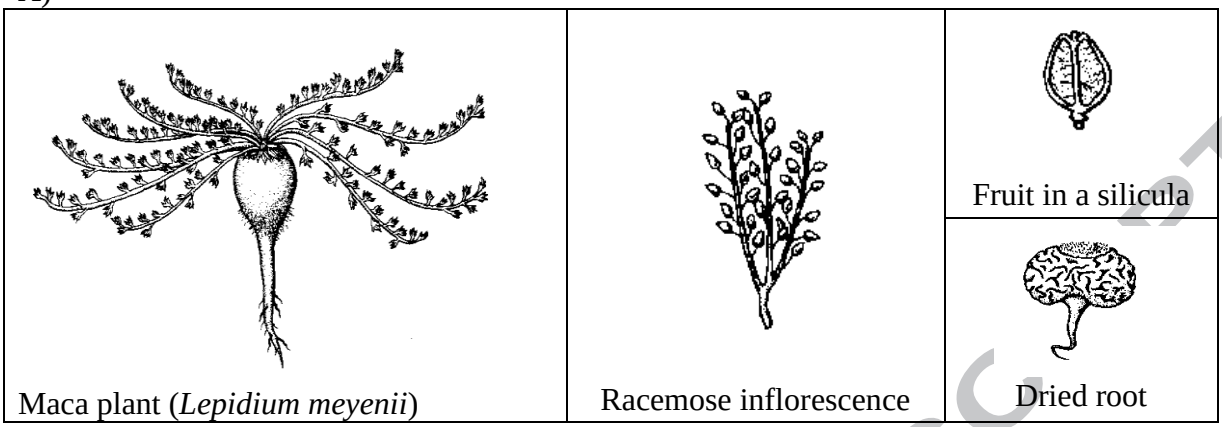
The authors declare no conflict of interest.

Figure captions

Figure 1. A) Maca (*Lepidium meyenii)* plant (Hernándo Bermejo & León, 1994); B) Yellow, purple and black maca roots (Chen et al., 2017). Figures are reproduced with permissions from the publishers

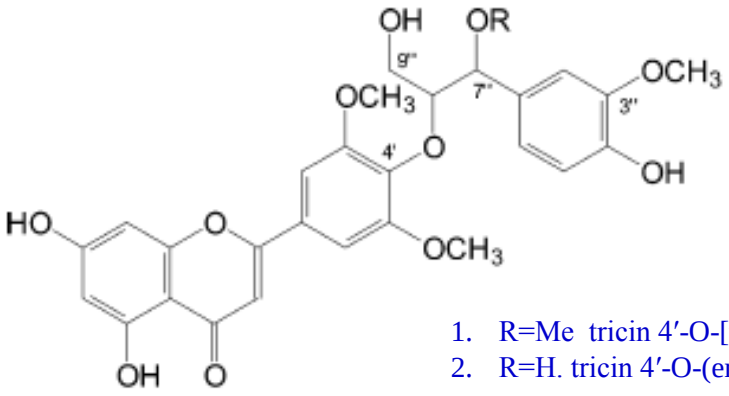
Figure 2. Chemical structures of representative bioactive components in maca. Figures are reproduced with permissions from the publishers

A)



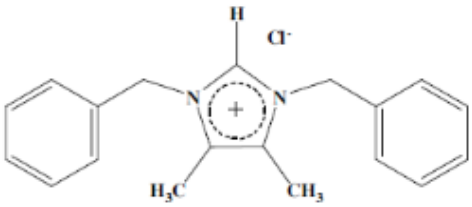
B)

Figure 1

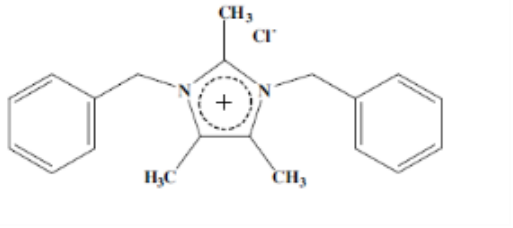


1. R=Me tricin 4′-O-[threo-β-guaiacyl-(7″-O-methyl)-glyceryl] ether
2. R=H. tricin 4′-O-(erythro-β-guaiacyl-glyceryl) ether

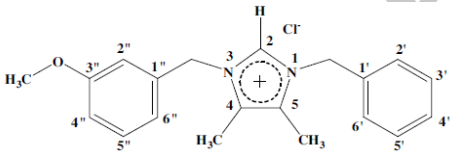
Flavonolignans (Bai et al., 2015)



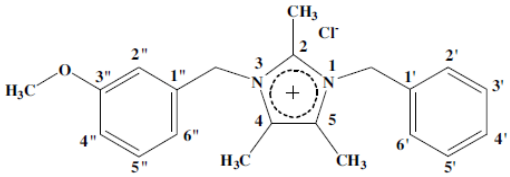
Lepidiline A



Lepidiline B

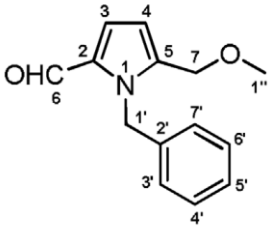


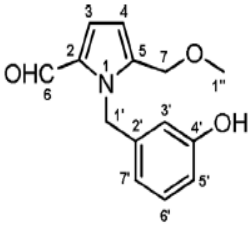
Lepidiline C

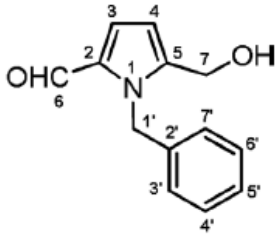


Lepidiline D

Imidazole alkaloids (Cui et al., 2003; Jin et al., 2016)

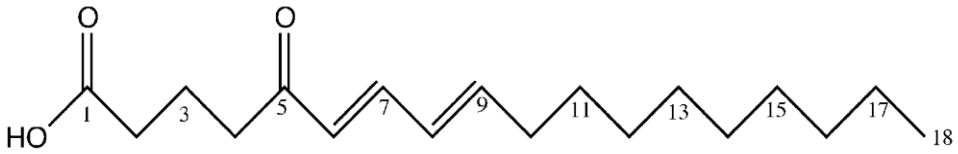






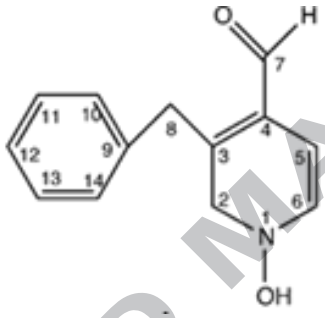
Macapyrrolin A Macapyrrolin B Macapyrrolin C

Pyrrole alkaloids (Zhou et al., 2018)

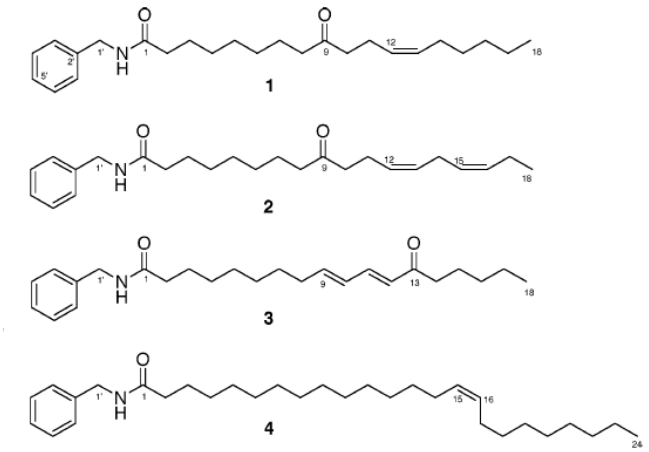


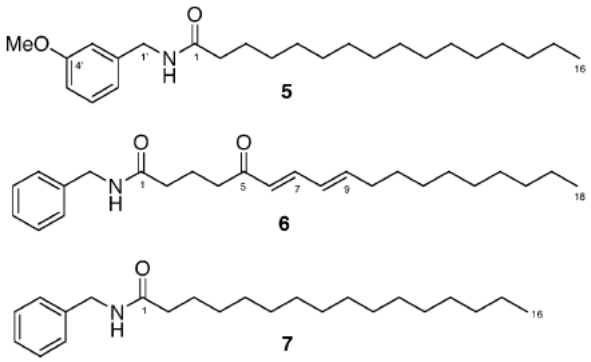
5-oxo-6E,8E-octadecadienoic acid

Acyclic polyunsaturated oxoacids (Macaenes) (Muhammad et al., 2002)



1,2-dihydro-N-hydroxypyridine derivative (Macaridine) (Muhammad et al., 2002)





1) N-Benzyl-9-oxo-12Z-octadecenamide
2) N-Benzyl-9-oxo-12Z,15Z-octadecadienamide
3) N-Benzyl-13-oxooctadeca-9E,11E-dienamide
4) N-Benzyl-15Z-tetracosenamide
5) N-(m-Methoxybenzyl)hexadecanamide

6) N-benzyl-5-oxo-6E,8E-octadecadienamide
7) N-benzylhexadecanamide

Alkamides (Muhammad et al., 2002; Zhao et al., 2005)

Table 1 Major and minor constituents of roots and aerial parts of maca

Chemical constituents	Root	Aerial parts[1] (leaf, stem, and inflorescence)	References
Nutritional composition			
Moisture (% wet basis)	4.63−10.40	79.79−88.50	Dini et al. (1994);Chen et al. (2 Jin et al. (2018)[1]
Protein (% dry basis)	9.56−21.90	23.02−38.48	Dini et al. (1994); Guo et al. (2 Jin et al. (2018)[1]
Amino acid composition (mg/g protein)			
Total amino acids	876.76−1255.33	13.306−24.442[3]	Chen et al. (2017); Jin et al. (20
Essential amino acids	189.19−312.90	41– 47[4]	Chen et al. (2017); Jin et al. (20
Threonine	24.75− 43.74	0.778−1.4112[3]	Chen et al. (2017); Li, Chen et
Valine	37.12−81.79	0.862−1.551[3]	Chen et al. (2017); Li, Chen et
Methionine	5.91−57.99	0.314−0.491[3]	Chen et al. (2017); Li, Chen et
Phenylalanine	24.37−55.30	0.827−1.451[3]	Chen et al. (2017); Li, Chen et
Isoleucine	24.78−47.40	0.179−1.328[3]	Chen et al. (2017); Li, Chen et
Leucine	35.10−91.0	1.210−2.109[3]	Chen et al. (2017); Li, Chen et
Lysine	36.29−61.01	0.894−2.149[3]	Chen et al. (2017);Li, Chen et a
Nonessential amino acids	634.44−942.43	INA	Chen et al. (2017);Li, Chen et a
Aspartate	54.16−91.70	0.763−2.751[3]	Chen et al. (2017);Li, Chen et a
Glutamate	61.58−156.5	1.276− 3.689[3]	Chen et al. (2017);Li, Chen et a
Serine	17.89−50.40	0.784−1.460[3]	Chen et al. (2017);Li, Chen et a
Histidine	15.29−34.25	0.365−0.678[3]	Chen et al. (2017);Li, Chen et a
Glycine	31.64−68.30	0.880−1.460[3]	Chen et al. (2017);Li, Chen et a
Arginine	76.47−238.91	1.099−2.055[3]	Chen et al. (2017);Li, Chen et a
Alanine	28.88−63.10	0.836−1.620[3]	Chen et al. (2017); Li, Chen et
Tyrosine	15.64−30.60	0.685−1.145[3]	Chen et al. (2017); Li, Chen et
Cysteine	1.37−2.93	0.010−0.109[3]	Chen et al. (2017); Li, Chen et
Proline	0.50−422.92	0.928−1.657[3]	Chen et al. (2017); Li, Chen et
Ratio of essential amino acids to total amino acids	0.21−0.28	INA	Chen et al. (2017); Chen et al. ((2017)
Crude lipids (% dry basis)	0.59−2.20	INA	Dini et al. (1994);
Saturated fatty acid (% lipids)	40.1[2]	INA	Dini et al. (1994)

Dodecanoic (lauric) C12:0	0.8[2]	INA	Dini et al. (1994)
Tridecanoic C13:0	0.1[2]	INA	Dini et al. (1994)
Tetradecanoic (myristic) C14:0	1.4[2]	INA	Dini et al. (1994)
Pentadecanoic C15:0	1.1[2]	INA	Dini et al. (1994)
Esadecanoic (palmitic) Cl6:0	23.8[2]	INA	Dini et al. (1994)
Heptadecanoic C17:0	1.8[2]	INA	Dini et al. (1994)
Octadecanoic (stearic) C18: 0	6.7[2]	INA	Dini et al. (1994)
7-Tridecenoic C13:1	0.3[2]	INA	Dini et al. (1994)
Nonadecanoic Cl9:0	0.4[2]	INA	Dini et al. (1994)
Eicosanoic (arachidic) C20:0	1.6[2]	INA	Dini et al. (1994)
7-Pentadecenoic C15:1	0.5[2]	INA	Dini et al. (1994)
Tetracosanoic (lignoceric) C24:0	0.4[2]	INA	Dini et al. (1994)
9-Esadecenoic (palmitoleic) C16:1	2.7[2]	INA	Dini et al. (1994)
Docosanoic (behenic) C22:0	2.0[2]	INA	Dini et al. (1994)
Unsaturated fatty acid (% lipids)	52.7[2]	INA	Dini et al. (1994)
9-Heptadecenoic C17: l	1.5[2]	INA	Dini et al. (1994)
9, 12-Octadecadienoic (linoleic) C18:2	32.6[2]	INA	Dini et al. (1994)
9-Octadecenoic(oleic) C18: 1	11.1[2]	INA	Dini et al. (1994)
11-Nonadecenoic C19:1	1.3[2]	INA	Dini et al. (1994)
15-Eicosenoic C20: l	2.3[2]	INA	Dini et al. (1994)
15-Tetracosenoic (nervonic) C24:1	0.4[2]	INA	Dini et al. (1994)
Saturated/unsaturated ratio	0.76[2]	INA	Dini et al. (1994)
Total carbohydrates (% dry basis)	46.1−74.8	INA	Dini et al. (1994); Guo et al. (2
Total starch (% dry basis)	37–77	INA	Rondán-Sanabria et al. (2012);
Total sugar content (% dry basis)	16.80−17.57[7]	1.01−2.21	Rondán-Sanabria et al. (2012);
Total dietary fiber (% dry basis)	15.60−26.00	INA	Guo et al. (2016); Chen et al. (2
Soluble dietary fiber (% dry basis)	2.46−7.88	INA	Chen et al. (2017)
Insoluble dietary fiber (% dry basis)	14.83−23.36	INA	Chen et al. (2017)
Ash (% dry basis)	3.41−4.9	INA	Dini et al. (1994); Li, Chen et a
Mineral composition (mg/kg dry basis)			
Potassium	5394.8−11700.0	3587.8−7527.5[6]	Chen et al. (2017); Li, Chen et
Calcium	3838.9−13700.0	1339.8−3231.4[6]	Chen et al. (2017); Li, Chen et
Magnesium	625.2−847.5	267.0−542.9[6]	Chen et al. (2017); Li, Chen et
Sodium	138.3−188.0	19.9−172.1[6]	Chen et al. (2017); Li, Chen et
Iron	58.1−550.3	17.9−84.3[6]	Chen et al. (2017); Li, Chen et
Zinc	23.3−30.7	INA	Chen et al. (2017); Li, Chen et
Manganese	9.8−17.1	INA	Chen et al. (2017); Li, Chen et
Copper	4.3−7.8	INA	Chen et al. (2017); Li, Chen et
Vitamin (mg/100g dry basis)			
Vitamin C	INA	162.9−236.3	Jin et al. (2018)[1]
Vitamin B3 (Niacin)	INA	35.2−134.5	Jin et al. (2018)1
Secondary metabolites, phytochemicals			
Total glucosinolates (nmol/kg, dry basis)	31.4–36.2 (1.24)[5]	6.25−18.13[5]	Yábar et al. (2011); Li, Chen et (2018)[1]
Total aromatic glucosinolates	30.96–35.90	INA	Yábar et al. (2011)

Glucosinalbin (4-Hydroxybenzyl glucosinolate)	0.58–1.03	INA	Yábar et al. (2011)
Glucotropaeolin (Benzyl glucosinolate)	25.2–29.1 (0.28-2.31)[5]	INA	Yábar et al. (2011); Chen et al.
Glucolimnanthin (3-Methoxybenzyl glucosinolate)	5.18–5.77	INA	Yábar et al. (2011)
Total indolyl glucosinolates	0.03–0.10	INA	Yábar et al. (2011)
4-Hydroxyglucobrassicin (4-Hydroxy-3-indolylmethyl glucosinolate)	0.01–0.04	INA	Yábar et al. (2011)
4-Methoxyglucobrassicin (4-Methoxy-3-indolylmethyl glucosinolate)	0.02–0.06	INA	Yábar et al. (2011)
Total aliphatic glucosinolates	0.23–0.28	INA	Yábar et al. (2011)
Glucoalyssin (5-Methylsulfinylpentyl glucosinolate)	0.23–0.28	INA	Yábar et al. (2011)
Total Alkaloids (mg/g dry basis)	0.17–2.99	INA	Chen et al. (2017); Li, Chen et
Total macamides (mg/g, dry basis)	0.392–2.950	0.451−0.703	Chen et al. (2017); Li, Chen et
N-benzylpalmitamide	0.130[2]	INA	Dini et al. (1994)
N-benzyloleamide	0.090[2]	INA	Dini et al. (1994)
N-benzyllinoleamide	0.083[2]	INA	Dini et al. (1994)
N-benzyl hexadecanamide	0.005–0.194	INA	Chen et al. (2017)
Total saponin (mg/g, dry basis)	INA	33.18−51.83	Jin et al. (2018)[1]
Sterols			
Sitosteryl acetate (% sterols)	45.5[2]	INA	Dini et al. (1994)
Campesteryl acetate (% sterols)	27.3[2]	INA	Dini et al. (1994)
Ergosteryl acetate (% sterols)	13.6[2]	INA	Dini et al. (1994)
Brassicasteryl acetate (% sterols)	9.1[2]	INA	Dini et al. (1994)
$\Delta^{7,22}$-ergostadienyl acetate	4.5[2]	INA	Dini et al. (1994)

[1,] aerial parts of maca (leaf, stem, and inflorescenc) at different growth stages; [2,] average values; [3,] g/100 g dry weight; [4,] % total amino acids; [5,] mg/g, dry weight, [6,] values of fresh weight; [7,] different storage days; INA, information not available.

Table 2 Bioactive polysaccharides isolated from maca leaves and roots

Polysaccharide	Isolation and purification method (Purity %)	Polysaccharide types (MW)	Monosaccharide composition (Molar ratio)	Typical FTIR wavenumber (cm^{-1})	Bioactivities (*In vitro/in vivo* models)	Reference
Leaf polysaccharide (MPL-1)	Water extraction. DEAE cellulose-52 and Sephadex G-200	Hetero-polysaccharide (42.756 kDa)	Rib, Rha, Ara, Xyl, Man, Glc, Gal (0.12:0.32:1.50:0.32: 1.03:1.00:0.93)	3500-3200, 2928 1629, 1395, 1200-1010 868, 573	Antioxidative (*In vitro* chemical model)	Kang et al. (2018)
Leaf polysaccharide (MPL-2)	Water extraction. DEAE cellulose-52 and Sephadex G-200	Homo-polysaccharide (93.541 kDa)	Glu (1)	3500-3200, 2926,1619, 1420,1200-1010, 863, 570	Antioxidative (*In vitro* chemical model	Kang et al. (2018)
Leaf polysaccharides (LMLP)	Water extraction ethanol precipitation and deproteinization. DEAE cellulose-52 and Sephadex G-100	Hetero-polysaccharide (58.43 kDa)	Gal, Ara, Rha, Glu, Man (5.51:4.05:1.15:0.77: 0.01)	3600-3200 3286.62, 2933, 1734.99, 1605.69, 800–1200, 1239.86 1020.29,535.7	Antioxidative (*In vitro* chemical model) Immunomodulatory (*In vitro* cell model)	Li, Hao et al. (2017)
Root polysaccharide (MPS-1)	Water extraction. DEAE-52 cellulose and Sephadex C-100 (93.2%)	Neutral Polysaccharide (7.6 kDa)	Xyl, ara, gal, glc (1:1.7:3.3:30.5)	3427, 1654 1411,1000-1200,860	Antifatigue (*In vivo* animal model)	Li, Sun et al. (2017)
Root polysaccharide (MPS-2)	Water extraction, DEAE-52 cellulose and Sephadex C-100 (91.5%)	Acidic polysaccharide (6.7 kDa)	Ara, gal, glc (1:1.3:36.8)	3417,3120, 1639,1396, 1257,1000-1200, 862 ,950	Antifatigue (*In vivo* animal model)	Li, Sun et al. (2017)
Root polysaccharide (MP-1)	Ultrasonic assisted water extraction. DEAE-52 (91.63%)	Hetero-polysaccharide (1067.3 kDa)	Rha, GalUA, Glc, Gal, Xyl, Ara (Not reported)	3322, 2928, 1651, 1416,1038 834	Antioxidative (*In vitro* chemical model) Hepatoprotective (*In vitro* cell and *In vivo* animal models)	Zhang, Zhao et al. (2017)
Root	Water extraction, ethanol	Acidic	D-Gala, D-Glc,	3404, 2931, 1738-	Antifatigue	Tang et al.

polysaccharides (MP)	precipitation and deproteinization. Sephacryl S-100 HR (99.2 %)	polysaccharide (793.5 kDa)	L-Ara, D-Man, D-Gal, L-Rha (35.07:29.98:16.98:13.01:4.21:0.75)	1634	(*In vivo* animal model)	(2017)
Tube polysaccharide (MCP)	Water extraction and ethanol precipitation (61.0%)	Hetero-polysaccharide	Rha, glc, gal (2.34:10.21:1.00)	Not reported	Antifatigue (*In vivo* animal model)	Li, Xin et al. (2018)
Root polysaccharide (MC-1)	Water extraction, ethanol precipitation and deproteinization. DEAE-Sepharose and Sephadex G-100 (97.5%)	Hetero-polysaccharide (11.3 kDa)	Ara, Man, Glu, Gal (26.21:11.81:53.66:8.32)	3406, 2927, 1637,1422,1043 897, 573	Immunomodulatory (*In vitro* cell model)	Zhang, Wang et al. (2016)
Root polysaccharides (MP21)	Water extraction, DEAE-52 and Sephacryl TM S-500 (90.5%)	Neutral polysaccharide (368 kDa)	Rha, Ara, Gal (1:4.84:5.34)		Immunomodulatory (*In vitro* cell model)	Wang, Zou et al. (2016)

DPPH, 2, 2-diphenyl-1-picrylhydrazyl; Ara, arabinose; Gal, galactose; Glc, glucose; GalUA, galacturonic acid, Man, mannose; Rib, ribose; Rha, rhamnose; Xyl, xylose; MW, molecular weight; table adapted from Li, Xin et al. (2018)

Table 3 *In vivo* and clinical experiments demonstrating effects of maca in sexual functions of male and female reproductive systems

Examples of effects	Type of maca product [extract concentration (EC); treatment dosage (TD) and length]	Tentative key bioactive	Reference
	Improving male spermatogenesis (animal trials)		
Increased frequency of stage VIII	Maca root aqueous extracts (EC: 67 mg/mL; TD:1 mL twice daily, 14 days)	Undetermined	Gonzales et al. (2001b)
	Black, yellow and red maca aqueous extracts (EC:166.7 mg/mL; TD: equivalent to 1g raw material/kg rat body weight, daily, 84days)	Antioxidants	Gasco et al. (2007a)
Increased length of stage VIII	Black and yellow maca aqueous extracts (EC:333.3 mg/mL; TD: 666.6 mg extract or 1.66 mg/kg rat body weight, daily)	Polyphenols, antioxidants	Gonzales et al. (2006a)
	Yellow maca aqueous extracts (lyophilised) (EC: 333mg/mL; TD:0.1-5g/kg daily, 7days)	Undetermined	Chung et al. (2005)
	Black maca ethyl acetate fraction EC:100g dried root yield 207.7mg extract; TD:1 dry extract/kg rat body weight, daily, 7days)	Polyphenols	Yucra et al., (2008)
	Black and yellow maca milled powder (EC: not available; TD: equivalent to 1 dry material/kg rat body weight, daily, 3days)	Total phenolics	Inoue et al. (2016)
	Black and yellow maca aqueous extracts (EC:166.7 mg/mL; TD:1 dry root/kg rat body weight, daily, 84 days)	Antioxidants	Gasco et al. (2007a)
Increased daily sperm production	Black maca aqueous extracts (EC:333.3 mg/mL; TD: 666.6 mg extract or 1.66 mg/kg rat body weight, daily, 42 days)	Polyphenols, antioxidants	Gonzales et al. (2006a)
	Black maca ethyl acetate fraction EC:100g dried root yield 207.7mg extract; TD:1 dry extract/kg rat body weight, daily, 7days)	Polyphenols,	Yucra et al. (2008)
	Black and yellow maca milled powder (EC: not available; TD: equivalent to 1 dry material/kg	Total phenolics	Inoue et al. (2016)

	rat body weight, daily, 3days)		
Increased sperm count in the vas deferens	Black, yellow and red maca aqueous extracts (EC:166.7 mg/mL; TD:1 dry root/kg rat body weight, daily, 84 days)	Secondary metabolites	Gasco et al. (2007a)
Increased sperm count	Maca ethanol extract (dried) (EC:28 and 48 mg/mL TD: 96 mg extract/day, daily, 21 days)	Undetermined	Gonzales et al. (2003b)
Increased epididymal sperm count	Maca aqueous extract (pulverised dried roots) (EC:333.3 mg/mL; TD:0.6−666.6 mg/day, daily, 21 days)	Essential amino acids (i.e., arginine)	Gonzales et al. (2004)
Altered pattern of daily sperm production	Black maca aqueous extracts (EC:333.3 mg/mL; TD: 2g dry root/kg rat body weight, daily, 12 days)	Undetermined	Gonzales et al. (2006b)
At high altitude exposure	Maca aqueous extract (pulverised dried roots) (EC:333.3 mg/mL; TD:0.6−666.6 mg/day, daily, 21 days)	Essential amino acids (i.e., arginine)	Gonzales et al. (2004)
At malathion exposure	Maca aqueous root extract (EC: 333.3 mg/mL; TD: 66.6 mg extract, daily, 21 days)	Undetermined	Bustos-Obregon et al. (2005)
At lead acetate exposure	Maca aqueous extract (pulverised dried roots) (EC:333.3 mg/mL; TD: 2.2 g extract/kg, 35 days)	Undetermined	Rubio et al. (2006)
Prostate size reduction	Red maca aqueous extract (EC:333.3 mg/mL; TD: equivalent to 2g dry root/kg rat body weight, daily, 42days)	Glucosinolates and its metabolites	Gonzales et al.(2005)
	Red maca EC: 333.3 mg/mL; TD: 666.6 mg extract, daily,42 days)	Undetermined	Gonzales et al. (2006a)
	Red maca aqueous and hydroalcoholic extracts (EC: 333.3 mg/mL; TD: 1 mL freeze dried aqueous extract or spray dried hydro-alcoholic extract, daily, 14 days)	Benzyl glucosinolate	Gonzales et al. (2007)

	Red maca aqueous extract (EC: 166.7 mg/mL; TD: 2g raw material/kg, rat body weight, daily, 14 days)	Undetermined	Gonzales et al. (2012)
Effect on stromal cells	Red maca hydroalcoholic extract (EC: 60% ethanol. TD: 140 mg red maca/ kg rat body weight, daily, 21days)	Polyphenols in aqueous extract or most polar fraction	Gonzales et al. (2008)
Zinc level regulation	Red maca aqueous extract (EC: 166.7 mg/mL; TD: 2g raw material/kg, rat body weight, daily, 14 days)	Undetermined	Gonzales et al. (2012)
Prostate weight reduction	Red and black maca (EC: not available; TD: 167mg maca/kg, rat body weight, daily, 21 days)	Undetermined	Noratto et al. (2013)
Erectile dysfunction treatment	Maca extract (EC: Polysaccharide rich extact, and macaene and macamides rich extract. TD: 45 mg extract/kg, rat body weight, daily, 22 days)	Polysaccharide, 0.6% macaene and macamides, benzyl isothiocyanate, *p* methoxy benzyl isothiocyanate	Zheng et al. (2000)
	Maca (EC: not available, TD: 100 mg/kg, rat body weight, daily, 8 weeks)	Undetermined	Kimura et al. (2016)
Decreased post-ejaculatory latency	Maca root (pulverised, standardized at 0.6% macaene and macamides) (EC: not available, TD: 75 mg extract/kg, rat body weight, daily, 15 days)	0.6% macaene and macamides	Cicero et al. (2001)
Increased mount latency	Maca hexanic, methanolic and chloroformic extracts (EC: 52mg hexanic extract, or 870 mg methanolic, or 24mg chloroformic extracts diluted in saline; TD: 0.5mL/kg, rat body weight, daily, 5 days	Benzyl glucosinolate	Cicero et al. (2002)
Premature ejaculation treatment	Maca aqueous extracts (EC: not available, TD: 25,100 mg /kg, rat body weight,	Undetermined	Lentz et al. (2007)

	daily, 21 days)		
Increased number of mounts and ejaculations	Maca ether, alcoholic and aqueous extracts Maca root (pulverised, standardized at 0.6% macaene and macamides) (EC: not available, TD: 4, 0.8 mg /kg, rat body weight, daily,6 days)	Non-polar alkaloids Aromatic isothiocyanates	Zhang et al. (2016)
Enhanced libido	Black maca (dried) (EC: not available; TD: 233mg/kg sheep ram body weight, daily, 16 weeks)	Undetermined	Lavana et al. (2013)
Increased sexual capacity	Black maca powder (milled) (EC: milled powder suspended in 250 mL water; TD: 233mg dry maca/ kg ram body weight, daily,4 weeks)	Undetermined	Avelar et al. (2016)
Increased ejaculation volume	Maca (Gelatinised) (EC: not available; TD: 300, 1500 mg/kg healthy man body weight, daily, 4 months)	Undetermined	Gonzales et al. (2001a)
Increased total sperm count	Maca (Gelatinised) (EC: not available; TD: 300, 1500 mg/kg healthy man body weight, daily, 4 months)	Undetermined	Gonzales et al. (2001a)
Increased motile sperm count	Maca (Gelatinised) (EC: not available; TD: 300, 1500 mg/kg healthy man body weight, daily, 4 months)	Undetermined	Gonzales et al. (2001a)
Increased sperm motility	Maca (Gelatinised) (EC: not available; TD: 300, 1500 mg/kg healthy man body weight, daily, 4 months)	Undetermined	Gonzales et al. (2001a)
	Maca pill (EC: not available; TD: 480 mg every 12 hours, healthy man, 50-62 years old, 3 months)	Undetermined	Poveda et al. (2013)
	Maca capsule (pulverized and dehydrated maca root) (EC: not available; TD: 3000 mg daily, males, 3 months)	Undetermined	Tancara et al. (2010)
Improved sperm quality	Maca hypocoty(dried milled) (EC: not available; TD: 1.75g daily, healthy males, 12weeks)	Undetermined	Melnikovova et al. (2014)

Improved semen quality and serum hormones	Yellow maca capsule (containing 350 mg gelatinised powder) (EC: not available; TD: 1.75g daily, healthy males, 12weeks)	Macamides n-benzyl-hexadecanamide, n-benzyl-(9Z.12Z)-octadecadienamide, and n- benzyl-(9Z.12Z.15Z)-octadecatrienamide	Melnikovova et al. (2015)
Increased sexual desire	Maca tablets (containing 500mg dehydrated roots) (EC: not available; TD: 1500, 3000 mg, daily, 8-12 weeks)	Undetermined	Gonzales et al. (2002)
Improved hypoactive sexual desire	Maca (EC: not available; TD: 480mg, every 12 hours, daily, 3 months)	Undetermined	Poyato et al. (2009)
Improved rating of dyadic sexual desire	Maca capsule (EC: not available; TD: 2000mg/day, daily, 14 days)	Undetermined	Stone et al. (2009)
Improved well-being performance	Maca tablet (pulverized and dehydrated roots) (EC: not available; TD: 2400mg/day, daily, 12 weeks)	Undetermined	Zenico et al.(2009)
	Improving female fertility (animal trials)		
Increased progesterone level	Maca powder (EC: 0.05g power/mL water; TD: 05g/mL, 30 days)	Saponins	Oshima et al. (2003)
	Maca powder (Pre-gelatinized) (EC: not available; TD: 0.75, 7.5 g/kg rat body weight, daily, 90 days)	Complex phytochemicals	Meissner et al. (2006a)
Increase number of pups	Yellow maca aqueous extract (lyophilized) (EC: not available; TD: 1g extract/kg rat body weight, daily, 15 days)	Undetermined	Ruiz-Luna et al. (2005)
	Maca methanol and pentane extracts (EC: not available; TD: 3, 30 mg/kg rat body weight, daily, 21 days)	Undetermined	Pino-Figueroa & Maher, (2009)
Increased pregnancy rates	Maca methanol and pentane extracts (EC: not available; TD: 3, 30 mg/kg rat body weight, daily, 21 days)	Undetermined	Pino-Figueroa & Maher, (2009)
Increased serum luteinizing hormone	Maca powder	Undetermined	Uchiyama et al.

level in pro-estrus	(EC: not available; TD: 3,15,30g/kg rat body weight, daily, 7 weeks)		(2014)
Improved anti-depression and cognitive function	Maca powder (Pre-gelatinized) (EC: not available; TD: 0.75, 7.5 g/kg rat body weight, daily, 90 days)	Complex phytochemicals	Meissner et al. (2006a)
Alternated uterine wet weight	Yellow maca aqueous extract (lyophilized) (EC: not available; TD: 1g extract/kg rat body weight, daily, 15 days)	Undetermined	Ruiz-Luna et al. (2005)
	Maca supplement (EC: not available; TD: 0.5265 mg, daily, 10weeks)	Undetermined	Barraza et al. (2015)
Protecting bone loss	Maca ethanol extract (lyophilised) (EC: not available; TD: 0.24 extract/kg rat body weight, daily, 28 weeks)	Calcium, magnesium, Silica and phychemicals	Zhang et al. (2006)
	Black and red hydroalcoholic extract (standardized at polyphenol content) (standardized at 0.6% macaene and macamides)	Polyphenols, poly-unsaturated fatty acids and phytosterols	Gonzales et al.(2010)
Balanced serum hormone	Maca ethanol extract (EC: not available; TD: 0.5, 1.25 power/kg rat body weight, daily, 7 month)	Undetermined	Zhang et al. (2008)
	Yellow maca powder (Pulverised) (EC: not available; TD: 1.8g power/kg rat body weight, daily, 7 weeks)	Undetermined	Wang et al. (2009)
	Maca ethanol extract (pulverised, standardized at 0.6% macaene and macamides) (EC: not available; TD: 0.096, 0.24g/kg rat body weight, daily, 28 weeks)	Undetermined	Zhang et al. (2014)
	Maca powder (Pre-gelatinized) (EC: not available; TD: 250 mg/kg rat body weight, daily, 28 days)	Undetermined	Meissner et al. (2006b)
Balanced serum lipid levels	Maca ethanol extract (EC: not available; TD: 0.5, 1.25 maca powderg/kg rat	Undetermined	Zhang et al. (2008)

	body weight, once, daily, 7months)		
	Maca supplement (EC: not available; TD: 0.5265 mg, daily, 10weeks)	Undetermined	Barraza et al. (2015)
Alleviated menopausal symptoms	Maca capsules (gelatinized) (EC: not available; TD: two 500mg hard capsules, twice, daily, 2 month)	Sterols	Meissner et al. (2005)
	Maca powder (Pre-gelatinized) (EC: not available; TD: two 500mg vegetable hard gel capsules, twice, daily, 4 month)	Undetermined	Meissner et al. (2006d)
	Maca Root (Pre-gelatinized and pulverized) (EC: not available; TD: two 500mg hard capsules, twice, daily, 2 month)	Undetermined	Meissner et al. (2006e)
Hormone balancing effect	Maca powder (Pre-gelatinized) (EC: not available; TD: two 500mg vegetable hard gel capsules, twice, daily, 3 month)	Undetermined	Meissner et al. (2006c)
Increased in bone density	Maca powder (Pre-gelatinized) (EC: not available; TD: two 500mg vegetable hard gel capsules, twice, daily, 4 month)	Undetermined	Meissner et al. (2006d)
Anti-depression effect	Maca powder (EC: not available; TD: 3.5g/day maca powder, 6 weeks)	Undetermined	Brooks et al. (2008)
	Maca powder (encapsulated) (EC: not available; TD: 3.3g/day encapsulated maca powder, 6 weeks)	Undetermined	Stojanovska et al. (2011)
Improved orgasm	Maca roots (EC: not available; TD: 1500mg maca roots, twice, daily, 4 weeks)	Undetermined	Dording et al. (2015)

Table 4 Bioactivities (non-sexual effects) of maca products and tentative active compounds responsible for the observed effect

Biological effects	Maca products (country of origin)	*In vitro/in vivo* model systems		Observations	T b
Anti-fatigue	Maca polypeptide	*Assay*	Forced swimming test	Polypeptide dose-dependently and positively modified physiological indexes of mice, including blood glucose, urea nitrogen and creatinine	P
		Model	Mice (40 healthy male)		
		Dosage	5, 10, 20g / L maca polypeptide content		
		Admi.	Orally		
		Duration	14 days		
	N-benzyl-oleamide, N-benzyl-oleamide (China)	*Assay*	Forced swimming test	N-benzyloleamide (40 mg/kg) was more effective than N-benzyl-linole-amide (40 mg/kg) prolonged swimming duration. N-benzyloleamide decreased lactic acid, blood ammonia, lactate dehydrogenase. Decreased liver glycogen and malondialdehyde in the brain, muscle, and liver. Increased liver non-esterified fatty acid, superoxide dismutase and glutathione peroxidase activities in the brain, muscle, and liver	N N
		Model	Balb/c mice (male)		
		Dosage	12, 40 mg/kg		
		Admi.	Intragastrically		
		Duration	21 days		
	Grounded powder of dried yellow maca root (China)	*Assay*	Forced swimming test	Dose-dependently prolonged swimming duration, increased liver glycogen content, and decreased blood lactic acid. 400 mg/kg was recommended dose 1200 mg/kg induced side effects	P
		Model	Kunming mice (160 males)		
		Dosage	40,400,1200 mg/kg bw/d		
		Admi.	Gavage (feeding needle)		
		Duration	30 days		
	Polysaccharide isolated from water extract of oven-dried maca roots (China)	*Assay*	Forced swimming test	Dose-dependently increased average swimming speed and prolonged swimming duration. 100 mg/kg most effectively enhanced the activities of serum antioxidants (glutathione peroxidase, creatine kinase lactate dehydro-genase), and decreased metabolic products (blood urea nitrogen, lactic acid, malondialdehyde)	P (
		Model	ICR mice (40 males, 40 females)		
		Dosage	25, 50, 100 mg/kg bw/d		
		Admi.	Orally		
		Duration	30 days		
	Polysaccharide (MPS-1 and -2) isolated from water extract of maca	*Assay*	Forced swimming test	Dose-dependently anti-fatigue (increased blood lactate, urea nitrogen, lactic dehydrogenase activity, and decreased liver glycogen.MPS-2 has a better anti-fatigue effect than MPS-1	P (k
		Model	Kunming mice		
		Dosage	20, 100 mg/kg bw/d		
		Admi.	Oral gavage		
		Duration	30 days		

	Polysaccharide (MCP) isolated from water extract of maca	*Assay* *Model* *Dosage* *Admi.* *Duration*	Forced swimming test Kunming mice (40 males) 150, 300, 600 mg/kg bw/d Oral gavage 30 days	Effective dose:150 mg/kg Increased exhaustive swimming time.Increased liver glycogen, decreased blood urea nitrogen, unaffected lactic acid	F
Anti-oxidative	Polysaccharide MP-1 ultrasonically extracted from maca Roots (China)	*Assay* *Model* *Doses* *Admi.* *Time*	Chemistry based assays Hydroxyl, superoxide anion, DPPH radicals, FRAP Not applicable Not applicable Not applicable	Dose-dependently increased scavenging rates of hydroxyl DPPH, superoxide anion radicals and FRAP value	F p (
	Polysaccharide MLP-1 and -2 extracted from maca leaves (China)	*Assay* *Model* *Doses* *Admi.* *Duration*	Chemistry based assays Hydroxyl, superoxide anion, DPPH radicals Not applicable Not applicable Not applicable	MLP-1 had DPPH radical scavenging rate of 62.01%, EC_{50} of 0.21 (superoxide assay), and 0.44 (hydroxyl assay) mg/mL. MLP-2 had DPPH radical scavenging rate of 59.67%, EC_{50} of 1.01 (superoxide assay) and 0.66 (hydroxyl assay) mg/mL MLP-1 had stronger scavenging effects *in vitro* on hydroxyl, superoxide anion and DPPH radicals with EC_{50} of 0.44, 0.21, and 0.82. mg/mL, respectively	L p (k 9
	Polysaccharide LMLP from leaves (China)	*Assay* *Model* *Doses* *Admi.* *Duration*	Chemistry based assays DPPH radicals, reducing power Not applicable Not applicable Not applicable	Dose-dependently anti-oxidative, with EC_{50} of 3.72 mg/mL (DPPH aassy) and reducing power (OD700 nm, 0.079 at 1 mg/mL)	L p (
Neuro-protective	Maca powder (Peru)	*Assay* *Model* *Doses* *Admi.* *Duration*	Behavioral and Tests ICR mice (middle-aged male) 500mg maca powder/kg body weight gavage 5 weeks	Improved spatial learning and memory, motor coordination and swimming endurance capacity. Increased the expression of sub-units of mitochondrial respiratory chain complex, and activate autophagy signaling in cortex	M
	Pentane extract of dried roots (Peru)	*Assay* *Model* *Doses* *Admi.* *Duration*	*In vitro* & *in vivo* Crayfish neuronal cells; Sprague–Dawley male rats 0.1, 0.3, 1, 3, 10, 30 µg/mL (cells); 3, 10, 30 mg/kg (rats) Add to cell culture, Intravenously injection (rats) 18 h (cells); 24 h (rats)	Protected crayfish neuronal cells against neurotoxic agent (H_2O_2) (EC_{50} of 2.8 µg/mL. 3mg/kg dose exhibited neuroprotective effect on the brain of rats in stoke condition. Different interaction of lipophilic constituents with different cellular targets led to the protective effects	A b a n u o (b c
	Methanol extract	*Assay*	AChE and BuChE inhibition	80% methanol elution fraction of	I

	of maca (Peru and China)	*Model*	MPTP-induced zebrafish	methanol extract and macamides were a neuroprotective fraction via inhibiting
		Doses	0.025 to 1000 μ g/mL	
		Admi.	Not reported	acetyl-cholinesterase (AChE) and
		Duration	2 days	butyrylcholinesterase (BuChE)
	Aqueous and hydroalcoholic extracts of black maca roots (Peru)	*Assay*	Behavioral performance AChE inhibition	Both extracts inhibit scopolamine-induced memory and learning
		Model	Kunming strain male mice	impairment. Inhibited
		Doses	0.50, 2.00 g/kg (aqueous); 0.25,1.00 g/kg (hydroalcoholic)	acetylcholinesterase (AChE) activity
		Admi.	Orally	
		Duration	35 days	
	Hydroalcoholic extract of back maca roots (Peru)	*Assay*	Behavioral performance	Dose-dependently inhibited ethanol-induced memory impairment during
		Model	Swiss strain male mice	the escape acquisition trials.
		Doses	0.125, 0.25, 0.50, 1.00 g/kg	Improved spatial learning and
		Admi.	Orally	memory in male mice treated with
		Duration	28 days	ethanol
	Aqueous extract of dried black maca roots (Peru)	*Assay*	Behavioral performance	Increased step-down latency,
		Model	Variectomized mice	decreased malonalehyde,
		Doses	0.50, 2.00 g /kg	acetylcholinesterase levels. Improved
		Admi.	Orally	experimental memory impairment
		Duration	35 days	
Hepato-protective	Polysaccharide MP-1extracted from maca roots (China)		In vitro and in vivo	*In vitro,* dose-dependently protected
		Model	Hep-G2 cell, ICR female mice	alcohol induced decreases of Hep-G2
		Dosage	0.125, 0.25, 0.5, 1, 2mg/mL (cell); 200, 600, 1800 mg/kg, bw (mice)	cells. *In vivo*, reduced alcohol increased activities of transaminases (aspartate transaminase, alanine
		Admi.	in cell culture; Orally (mice)	aminotransferase, gamma- glutamyl
		Duration	24h (cells); 28 days (mice)	transpeptidase). Increased alcohol reduced superoxide dismutase, glutathione peroxidase, glutathione s-transferase
Antiviral	Methanol extract of maca root powder (Peru)	*Assay*	MTT	Methanol extract (≤ 200 μg/mL) were
		Model	Madin-Darby canine kidney (MDCK) cells human influenza Type A (Flu-A) and Type B (Flu-B) virus	non-toxic to normal MDCK cells (CC_{50} of extract were 850 μg/mL Methanol extract (10-80 μg/mL) Inhibited virus of human Flu-A (IC_{50}
		Doses	0-1000 μg/mL	of 5.4 μg/mL) and Flu-B (IC_{50} of 7.69
		Admi.	Added to cells	μg/mL) growth in MDCK infected
		Duration	6 days	cells.
Anti-cancer	Aqueous extract of red maca (Peru)	*Assay*	MTT	20 and 40 μg/mL stimulateed
		Model	LNCaP cells	androgen signalling in LNCaP cells
		Doses	0, 20,40, 80 μg/mL	via increasing mRNA expression of
		Admi.	In cell culture	Ar and Psa
		Duration	24 or 48 h	
	Isolated	*Assay*	MTT	tricin 4′-O-[threo-β-guaiacyl-(7″-O-

	component of maca roots	*Model* *Doses* *Admi.* *Duration*	Hep G2, COLO 205, and HL-60 cancer cells various concentrations In cell culture 24 h	methyl)-glyceryl] ether, tricin and lepidiline B were aniti-perliferative against HL-60 cells with IC_{50} values of 40.4, 52.0, and 52.1 μM, respectively	t [g n e l
Anti-inflammation	Isolated flavonolignans, lepidiline B	*Assay* *Model* *Doses* *Admi.* *Duration*	Nitrite production inhibition RAW 264.7 macrophage 20, 40 μg/mL In cell culture	40 μg/mL inhibited nitrite production in LPS-induced nitrite production in RAW 264.7 Macrophage	F t [g n e F
Immune-regulatory	Polysaccharide MC-1 from maca roots (Peru)	*Assay* *Model* *Doses* *Admi.* *Duration*	MTT RAW264.7 cells 62.5, 250, 1000 μg/mL In cell culture 6h	MC-1 (<1000 μg/mL was nontoxic to cells. MC-1 enhanced the pinocytic and phagocytic capacity to *E. coli* (FITC-labeled) of cells. MC-1 promoted release of NO and cytokines (IL-6, IL-10 and TNF-α) by targeting toll-like receptor 2, complement receptor 3, and mannose receptor	F p (
	Polysaccharide LMLP from maca leaves (China)	*Assay* *Model* *Doses* *Admi.* *Time*	MTT, phagocytosis activity RAW264.7 cells 10–160 μg/mL In cell culture 24h	LMLP (10–160 μg/mL) stimulated the proliferation of RAW264.7 cells, increased the cell phagocytosis. induced NO secretion, and promoted the expression levels of CD80	L p (
Preventive effects ultraviolet (UV) radiation	Maca roots extracts	*Assay* *Model* *Doses* *Admi.* *Time*	*In vivo* Male Holtzman rats 0.13 mg/mL applied on the dorsal surface 3 weeks	Maca roots extracts exhibited UV blocking activity. Boiled extracts had a better prevention effects than extracts without boiling	F g a
Gastro-intestinal motility promotion	Aerial parts of maca (APM)	*Assay* *Model* *Doses* *Admi.* *Time*	*In vivo* male and female Kunming mice 2.16, 1.08, 0.54 g/kg by gavage 7 days	APM stimulated gastric emptying, intestinal propulsion, endocrine cells of gastric sinus and duodenal to increase serum gastrin and motilin secretion, smooth muscle contraction, and the creep of the gastrointestinal tract.	F is

Admin., administration; CC_{50}, 50 % cytotoxic concentration; CD80, cluster of differentiation 80; EC_{50}, half maximal effective concentration; FRAP, ferric-reducing antioxidant power; IC_{50}, half maximal inhibitory concentration; LPS, lipopolysaccharides; MPTP, 1-methyl-4-phenyl-1, 2, 3, 6-tetrahydropyridine;MTT, 3-(4, 5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; NO, nitric oxide.

Highlights

- Functional components in root and aerial part of maca were characterized
- A variety of biological and pharmacological activities of maca were studied
- Diversifying maca derived ingredients for food and non-food uses was described
- Relationships between composition and bioactivity of maca components were discussed
- Maca has great potential to developed as a sustainable crop for human uses