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Aristotelia chilensis: A Possible Nutraceutical or Functional Food

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Abstract

Aristotelia chilensis (Maqui) is a native berry from Chile that has a wide range of biological actions. It is mainly composed of anthocyanins, indole alkaloids and flavonoids. However, the high concentration of polyphenols has been identified as the main responsible for the anti inflammatory, analgesic and antioxidants effects of their extracts, juices and fruit. The nutraceuticals or functional foods development is an excellent opportunity to make a nutritious and healthy product. This review includes the chemical and nutritional characteristics of Maqui. The pharmacological and biological activities are included in this work. Also shows our need to develop new healthy products

Keywords: *Aristotelia chilensis*; Nutraceuticals; Antioxidants; Antidiarrheal; Anthocyanins

Introduction

A nutraceutical is a product made from a food, which besides having a nutritional role by providing nutrients and energy, is capable of delivering the body other active ingredients beneficial to health, differing from a functional food in the form of presentation and administration [1].

In recent years, both in the market of American nutraceuticals as in Chile, there have been a number of products whose formulation containing *Aristotelia chilensis*. This fruit and leaves have shown a important range of biological actions, including antioxidants, anti-inflammatory and analgesic effects. These effects have led to use these products as complementary therapeutic agents in the treatment of various chronic and degenerative disorders. The fruits of *Aristotelia chilensis* have a high content of anthocyanins, of indole alkaloids and flavonoids, which makes them an attractive resource to produce antioxidant extracts for use in functional foods or nutraceuticals [1,2].

The *Aristotelia chilensis* (Mol.) Stuntz, belongs to the family of Elaeocarpareae, a Chilean native species, popularly known as Maqui. It is a small tree that does not grow beyond 4-5 meters high, evergreen, with reddish stems, thin, flexible branches. Its bark is smooth and soft. Its leaves are stalked, lanceolate, with serrated edges, measuring 4-9 cm. It has small, whitish flowers arranged in axillary inflorescences. Its fruits are small berries of about 5 mm, bright blue or black color. The Maqui grows wild and is distributed from Limarí in Region IV to Region XI Aysén in Chile. It thrives in moist soil, invading ravines, slopes of hills and forest edges [1-4].

In Chile, this species is known for the use given to the fruit in the diet. However, little has been used for medicinal purposes [5]. Only native peoples (mainly Mapuches) have used its leaves as a tea for therapeutic purposes in the treatment of diarrhea, acute tonsillitis, throat and mouth ulcers [6].

In recent years there has been an active interest in the berries, which are a group of fruits red, violet or purple, with a high content of polyphenols. Among the highlights are cranberries, myrtle, raspberries, grapes, caulk and also maqui or blackberry [7].

Traditional Medical Purposes

Among the traditional medicinal uses, fruits and juices, as well as Maqui leaves have been used [1,6,8]. Internally, the fruits have been used as a tonic that has antidiarrheal, anti-inflammatory, healing, digestive, diaphoretic, expectorant, laxative and diuretic properties. Infusions of the leaves can be administered as gargling in inflammation of the oropharyngeal mucosa [8]. The Mapuches used the fruits of maqui externally to treat infected wounds and burn dry leaves as healing [1,6,8].

Nutritional Composition

In 1990 Schmidt-Hebbel et al. published tables of chemical composition of Chilean foods where maqui is included as a native fruit [9]:

Schmidt- Hebbel et al. Composición Química de Alimentos Chilenos, 8°Edición. Universidad de Chile. According to Damascos et al. the maqui contains a significant amount of ascorbic acid. Native shrub fruits had higher content of Br, Zn, Co, Cr, Fe, Mo, and Na than those of the exotic naturalized species The fruit nutrient content found in the studied species was similar or higher than other values reported for fruits of temperate and tropical species in the world [10].

Maqui mature leaves contain a lower amount of potassium than the young leaves and increased sodium content. The content of magnesium, chlorine, calcium, titanium and vanadium does not vary between leaves of different sites with different annual rainfall [1].

Chemical Composition

The Maqui has mainly anthocyanins, indole alkaloids, flavonoids, coumarins [11] caffeic and ferulic acid [12]. However, it has released the presence of gallic acid, gentisic, sinapic, hydroxybenzoic, vanillic, makonine, 8-oxo-9 dehydrohobartine and 8-oxo-9 dehydromakomakine [11,13].

Anthocyanins, flavonoids and phenolic acids are compounds which occur very often in many plant families. Their different biological activities, including antioxidant, antimicrobial, carcinogenic, cytotoxic,

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anti-inflammatory and mutagenic properties, make them interesting objects of research [2].

The most revealing anthocyanidins are 3-glycosides, 3,5-diglycoside, 3-sambubioside 5- and 3-glycosides sambubioside of cyanidin and delphinidin. The anthocyanidin at higher rates proved to be the delphinidin 3-glucoside sambubioside-5 (34% of total) [14,15].

The most important flavonoids are quercetin 5,3'-dimethyl ether, malvidin, petunidin, friedelin and ursolic acid. It has also been obtained in the methanol extract; quercetin 3-O-B-D- glucoside y kempferol [1,12,15].

Among the indole alkaloids identified include the following: aristone, aristoletine, aristotelinone, aristotelone, aristoteline, aristotelinine, protopine, serratoline, hobartinol, 8-oxo-9-dehydro-hobartine, makonine, 8-oxo.9-dehydromakomakine, 9-dehydro-8-oxo-makomakine [16-18].

Pharmacological Activities

Antioxidant activity

Polyphenolic compounds maqui fruit have shown to possess potent antioxidant effects *in vitro* [19,20]. Maqui juices showed prevent lipid peroxidation induced by copper on human endothelial cells. The mechanism is explained by the effect of polyphenols maqui juice and by their antioxidant effect against oxidative stress [21].

Similarly, combining maqui juice with lemon juice important antioxidant effect against DPPH radicals, superoxide anion and hydroxyl were evidenced. The results suggested that lemon juice enriched with berries could be of potential interest in the design of new drinks with a nutritive related function on health for chronic diseases [22].

The new isotonic blends with lemon and anthocyanins-rich berries showed an attractive colour, especially in maqui samples, which is essential for consumer acceptance. Significantly higher antioxidant and biological effects were determined in the new blends, in comparison with the commercial isotonic beverages [23].

In general, aqueous and methanolic extracts of the fruit of the *A. chilensis* have shown antioxidant effects on *in vitro* models and xanthine oxidase inhibiting DPPH, fluctuating in the range of 52.9 and 62.7% respectively [12].

Crude extracts of leaves and fruits also showed antioxidant activity. Their polyphenols inhibit alpha-glucosidase enzyme. This enzyme is essential for the metabolism of carbohydrates and using these crude extracts, can be a useful mechanism in the management of diabetic patients. However, is necessary to make more research for warrants a potential dietary use of this berry in therapies to combat diabetes symptoms [24,25].

The Anthocyanins from *A. chilensis* improve fasting blood glucose levels and glucose tolerance in obese diabetic mice. Decreased glucose production and enhanced insulin-induced gene expression of glucose-6-phosphatase was observed in liver cells. For other hand, the Delphinidin 3-sambubioside-5-glucoside (D3S5G) was identified as principal anthocyanin of Maqui berry and responsible for these effects on glucose utilization [25,26].

The Aristoteline, aristone, serratoline and hobartinol were isolated from mixture of alkaloids (ALK-MIX). Ursolic acid, friedelin and quercetin 5,3'-dimethyl ether were present in the dichloromethane extract while quercetin 3-O-β-D-glucoside and kaempferol were present in the methanol extract. From aqueous extract (INFU) were isolated protopine, aristoteline and caffeic and ferulic acids. The effects of *A. chilensis* are here in demonstrated, validating its use in traditional medicine. Protopine was reported for the first time in Elaeocarpaceae for Muñoz in 2011[12].

Phenolics compounds are well-known antioxidants and their regular ingestion contributes to improve antioxidant status of plasma. Phytochemical findings describe phenolics compounds of leaves in *Aristotelia chilensis* (Molina) Stuntz, show that their administration in herbal teas may support the prevention of diseases whose etiology lies in the oxidative stress. The extracts obtained with polar solvents showed the stabilizing capacity of free radicals and the antioxidant capacity of plasma which, after taking *A. chilensis* tea, increased to 30.27% as an average. Herbal tea and extracts from *A. chilensis* exhibited antioxidant capacity under the described conditions [5]. The methanol extract (MeOH) from mature fruits of *Aristotelia chilensis* (Mol) Stuntz, showed antioxidant activities and cardioprotective effects on acute ischemia/reperfusion in rat heart *in vivo*. On the other hand, the methanolic extract of the fruits was able to prevent theses harmful events in the animal's heart by diminishing lipid oxidation. Antioxidant activities of MeOH were strongly correlated with total polyphenol content. Consistent with this finding, MeOH had the greatest ORAC and FRAP values as percentage of activity. These results show that these fruits could be useful as antioxidant, cardioprotective and nutraceuticals sources (Table 1) [27]. The presence of the compound indole-3-OH showed significant antioxidant effects and may explain the chemopreventive, anti-inflammatory and cardiopreventive activities this fruit [2].

Anti-inflammatory and analgesic activities

Folk medicine attributes to the leaves of this species, analgesic and anti-inflammatory properties to be backed by scientific studies and has also determined that the leaves have antimicrobial and antioxidant activities [3,12,28]. The lack of effective and safe long-term therapies to treat the inflammatory process is an important problem in animal health. Thereby, the discovery of new anti-inflammatory alternatives is imperative. We have determined the anti-inflammatory effects of *Aristotelia chilensis* fruit concentrate in rats subjected to subplantar acute inflammation induced by carrageenan [29].

A bioguided study was carried out on serial extracts (hexane, dichloromethane, methanol, INFU and crude ALK-MIX). All extracts were evaluated for: a) topical administration against both arachidonic acid and 12-deoxyphorbol-13-decanoate (TPA)-induced inflammation in mice b) per-os administration against inflammation by delta-carrageenan- induced paw oedema in guinea-pigs and c) topical analgesia in tail flick and formalin model and per-os writhing test in mice. Greater anti-inflammatory effects were obtained against TPA with dichloromethane extract and methanol extract (63.9% and 66% respectively). INFU showed the most potent effect (56.2%) against arachidonic acid. Greater effects were obtained in the writhing test hexane and dichloromethane extracts (89.2%) [12].

In the topical analgesia models, all the extracts and ALK-MIX and the methanol extract were the most active (58.2 and 55.2%, respectively). In relation to the tail formalin assay, the methanol extract (74.1%) was the most active [12].

Calories	Protein	CHO	Fibre	Ash	Calcium	Phosphorus	Iron	Potasium
150	0.8 g	40.8 g	0.8 g	1.2 g	87 mg	44 mg	30.5 mg	296 mg

Table 1: Nutritional composition of *Aristotelia chilensis* in 100 g of edible part.

The proposed mechanism of action for analgesic activity of the hexane extracts, is considered which would be modulated by L-arginine serotonergic receptors (5-HT3), adrenergic (a-1), cholinergic-muscarinic (ACh-M) and via/NO (nitric oxide). Instead antinociceptive activity of dichloromethane extract would be modulated by the opioid, serotonergic, adrenergic and nitridergic pathways. In the analgesic effect of methanol extract were involved the opioid systems, adrenergic, muscarinic cholinergic and L-arginine/NO. Alkaloids (Aristone, aristotelone, aristoteline and aristotelinine) demonstrated relax intestinal smooth muscle, explaining its anti-inflammatory and antispasmodic actions [3,28].

In general these compounds that occur in these Aristotelia species have been considered as the active principles of many anti-inflammatory plants. Thus, many phenolic acids, anthocyanins and flavonoids type have shown inhibitory activities on nitric oxide implicated in physiological and pathological process as chronic inflammation. These finding shows that the anthocyanins, flavonoids and phenolic acids may be responsible of the anti-inflammatory activity of this fruit. Actually, researchers are working in the kinetic of inhibition of these plant extracts and compounds as anti-inflammatory and they are dissecting the sites and mechanism of action as iNOS, Cyclooxygenase (COX), and TNF, among others [14].

Likewise, these extracts were able to reduce the production of nitric oxide (3.7-25.5%) and prostaglandin E2 (9.1-89.1%) and the expression of inducible oxide nitric synthase (9.8-61.8%) and cyclooxygenase-2 (16.6-62.0%) in RAW 264.7 macrophages stimulated by lipopolysaccharide [30].

Anthocyanins have effect during the inflammatory process, since they act by inhibiting the COX. Besides its antioxidant purpose and it inhibits adhesion of leukocytes to endothelial reaction to suppress the expression of molecules VCAM cells. They also inhibit mast cell degranulation and decreased levels of IL-2, IFN-y, and TNF-α [31].

It has been shown that anthocyanins inhibit the secretion of inflammatory cytokines such as IL-8, MCP-1, IL-1B-1 in neutrophil chemotactic cytokine-induced and IL-6 in cell and animal model after an inflammatory stimulus [32,33]. This suggests that it is feasible to use a formulation of dermatological use with *A. chilensis* to treat inflammatory skin diseases such as rosacea, sunburn and more circumscribed inflammatory lesions [34]. Other studies have suggested that supplementation with anthocyanins *in vivo* inhibits activation of NF-kB regulates many pro-inflammatory chemokines, cytokines and inflammatory mediators [35].

Anthocyanins exhibit a wide range of antioxidant protection and beneficial therapeutic effects including genomic DNA integrity, cardiovascular protection, neurological protection, anti-inflammatory and anti-cancer and can significantly reduce the production of NO, reducing oxidative stress in the anti-inflammatory process [29].

Others biological activities of general interest

A few years ago, the effects of concentrated of *A. chilensis* on the expression of COX-2, their signaling pathways and cell viability of colon cancer was assessed. Treatment of Caco-2 cells with *A. chilensis* for 24 hours reduced the expression of the protein and mRNA of COX-2, and reduced the luciferase activity regulated by NF-κB or NFAT.

Treatment of Caco-2 cells for 4 hours with *A. chilensis* temporarily reduced IκBα cytoplasmic levels, increased phosphorylation of ERK1/2 and Akt and the expression of c-fos. Also cell viability at concentrations that reduced expression of COX-2 was not affected. These results suggest a potential anticancer and anti-inflammatory effect [36].

On the other hand, the tannins of the fruit of the maqui have astringent properties and anti-diarrheal and the polyphenols of the leaves showed effects anti-hemolytic *in vitro* [24].

An experimental study evaluated the neuroprotective potential of an extract made from maqui polyphenols in Alzheimer's disease model induced by soluble oligomers B-amyloid.

Neurons cultures of rat hippocampus were used and neuroprotection was observed when neurons were incubated with amyloid B (0.5 uM) more maqui extract for 24 hrs. In the mechanism of action was observed a recovery in the frequency transients calcium channel, compared with the control group receiving only B-amyloid (Only B-amiloide=72 ± 3% and B-amiloide+Maqui= 86 ± 2%; n=5). This was positively correlated with observed in spontaneous synaptic activity and the preservation of dendritic branches changes. The antioxidant activity of maqui is primarily responsible for these changes [37]. Alzheimer's disease is characterized by the presence of different types of extracellular and neurotoxic aggregates of B-amyloid. Recently, bioactive compounds extracted from natural sources showing neuroprotective properties have become of interest in brain neuroregeneration. The results suggest that the maqui induces changes in the aggregation kinetics of Aβ producing variations in the nucleation phase. In conclusion, the maqui induces a potent neuroprotection by direct interaction with the B-amyloid aggregates, generating far less toxic species and in this way protecting the neuronal network [37].

The use of methanol extract of the ripe fruit provides cardioprotective activity in models of acute ischemia reperfusion in an *in vivo* study in rats [27]. Metabolically, has been evaluated *in vitro* the ability the some extracts of maqui, in reducing adipogenesis and lipid accumulation in adipocytes. In this regard, the phenolic extracts showed inhibit lipid accumulation between 4 to 10.8% in mature adipocytes and between 5.9 and 37.9% in those in differentiation state [1,38]. Concentrated juice of *Aristotelia chilensis* has a high content of phenolic compounds with antioxidant capacity, which protect both LDL from oxidation and endothelial cells from intracellular oxidative stress, suggesting that *Aristotelia chilensis* could have anti atherogenic properties [36].

Obesity is characterized by an increase in the infiltration of monocytes into the adipose tissue, causing an inflammatory condition associate with, for example, the development of insulin resistance. Thus, anti-inflammatory based treatments could emerge as a novel and interesting approach. It has been reported that Chilean native fruits maqui (*Aristotelia chilensis*) and calafate (Berberis microphylla) present high contents of polyphenols, which are known for their antioxidant and anti-inflammatory properties. The extracts of theses fruits present important inhibitory-like features over the inflammatory response of the interaction between adipocytes and macrophages, comprising a potential therapeutic tool against comorbidities associated with obesity development [39].

One study showed the protective effect of topical formulations containing quercetin on damage caused by oxidative stress induced by ultraviolet radiation. Two different formulations were used; a non-ionic emulsion with high lipid content and other anionic emulsion with low concentration of lipids. The results showed that the inflammatory damage induced by ultraviolet radiation decreased with both formulations, with better results when using non-ionic formulation rich in lipids [34].

In search of a nutraceutical formulations or a functional food based on *A. chilensis*

Infusions of its leaves have long been used in the traditional native

herbal medicine to treat different ailments. Phytochemical studies of chemical composition of the plant indicate the presence of indolic alkaloids, flavonoids, cianidine glucosides, delfidine, malvidine, petunidine, cumarines and triterpenes. These compounds, particularly the flavonoids, have antioxidant properties. In order to evaluate the mechanisms of its toxicity and their antioxidant properties, the leaves aqueous extracts were induced to interact with human red cells, their isolated unsealed membranes (IUM), and molecular models of the human erythrocyte membrane. Results of the study indicate that aqueous extracts of *A. chilensis* induced an alteration of human erythrocyte morphology from the normal discoid shape to an echinocytic form, changes that are explained in terms of the extract interaction with the membranes outer phospholipid monolayer .

In recent years, the food industry has shown great interest in developing maqui juice for its extraordinary potential as an antioxidant and functional food. In this sense, the development of a nutraceutical made from *A. chilensis* seems a logical step to have a product rich in polyphenols, flavonoids and anthocyanins [40].

For the evaluation of products and chemical characterization of the nutrients and healthy compounds, the quality of the product in dry and fresh should consider [41,42].

1) Drying and juice production substantially affected the stability of maqui anthocyanins

2) Stability of cyanidin and delphinidin derivatives differed during processing.

3) Maqui pomace was a valuable source for obtaining polyunsaturated fruit oils.

4) Maqui products exhibited nutritionally relevant mineral and trace element levels.

Increased domestic and international demand of maqui since 2006, increasing from 733 kg to more than 50,000 kg in 2011 (data from Chile Foundation 2012) showing the interest in this fruit [7].

The maqui has been used to make jams, fresh juices with water and sugar or functional foods by providing a number of compounds potentially beneficial for the health and rich in Polyphenolics components. The physical and chemical characteristics of the maqui juice with and without added sugar are showing in the Table 2 (from a study by Araneda et al. at the School of Agronomy of the Catholic University of Temuco, Chile) [40] .

Evidently, the total polyphenols content is not always the same, can be higher or lower depending on the ripeness of the fruit at harvest time, the type of climate, storage conditions and genotype [4,43].

Parameter	Juice with sugar	Juice without sugar
Soluble solids (°Brix)	22 ± 1.87	14 ± 1.79
pH	3.78 ± 1.03	3.35 ± 0.23
Acidity (%)	0.95 ± 0.13	0.85 ± 0.14
Humidity (%)	75.22 ± 1.49	86.6 ± 0.84
Dry matter (%)	24.78 ± 0.27	13.4 ± 0.13
Ash (g)	0.51 ± 0.02	0.44 ± 0.04
Sacarose (g 100mL^{-1})	19.32 ± 1.71	16.57 ± 0.65
Reducted sugars (g 100mL^{-1})	39.66 ± 1.90	6.8 ± 0.22
Total invert sugar (g 100mL^{-1})	58.98 ± 1.98	23.37 ± 0.69
Crude protein (%)	0.40 ± 0.01	0.19 ± 0.01
Total Polyphenols (mg 100 mL^{-1} EAG)	829.22 ± 25.86	993.21 ± 54.87
Total Polyphenols (mg EAG g^{-1} MS^{-1})	33.46 ± 2.22	74.1 ± 1.08
Total Carbohydrates (%)	3.41 ± 0.47	1.51 ± 0.44

Table 2: Physical-chemical analysis obtained maqui juice with and without sugar (40).

The maqui is characterized as an important source of phenolics compounds [24] and a product with a high content of polyphenols of natural origin, is a healthy product and considered functional [44].

The fruit of the maqui is considered the healthiest berry exotic, because of its particularly high concentration of bioactive polyphenols [27,38] and the use of this fruit rich in polyphenols in preparing of other foods, showed a reduction in the use of artificial additives antioxidants obtaining thus healthier foods [44,45].

The polyphenols, can prevent heart disease, by possessing vasodilatory effects, antibiotics, anti-inflammatory, anti-apoptotic, anti-atherogenic. Also could be prevent colon cancer [36,46], and providing a possible protective effect in preventing diseases of the retina [47]. Regardless of the course to follow; develop functional foods or nutraceuticals, the Maqui is a super food capable of providing innovative alternatives in food and natural product for health.

References

1. Alonso J (2012) Maqui (Aristotelia chilensis): Un nutraceutico chileno de relevancia medicinal. Rev Farmacol Chile 5: 95-100.
2. Cespedes CL, Alarcon J, Valdez-Morales M, Paredes-Lopez O (2009) Antioxidant activity of an unusual 3-hydroxyindole derivative isolated from fruits of Aristotelia chilensis (Molina) Stuntz. Z Naturforsch C 64: 759-762.
3. Fredes C (2009) Antioxidantes en berries nativos chilenos. Boletin Latinoamericano y del Caribe de Plantas Medicinales y Aromaticas 8: 469-478.
4. Fredes C, Montenegro G, Zoffoli J, Gomez M, Robert P (2012) Polyphenol content and antioxidant activity of maqui (Aristotelia chilensis (Molina) STUNZ) during fruit development and maturation in central Chile. Chilean Journal of Agricultural Research 72: 582-589.
5. Avello M, Valladares R, Ordonez J (2008) Capacidad antioxidante de Aristotelia chilensis (Molina) Stuntz. Rev Cubana Plant Med 13.
6. Munoz O, Montes M, Wilkomirsky T (2004) Aristotelia chilensis (MOL) STUNZ, En: Plantas Medicinales de uso en Chile. Quimica y Farmacologia, Ed. Universitaria, 2.
7. Fundacion Chile (2012) Demanda de maqui crece en forma exponencial. Disponible.
8. Chile. Ministerio de Salud (2009) MHT. Medicamentos Herbarios Tradicionales. 103 Especies Vegetales. Recuperado de.
9. Schmidt H (1992) Tabla de composicion quimica de alimentos chilenos. . Facultad de Ciencias Quimicas y Farmaceuticas. Departamento de Ciencias de los Alimentos y Tecnologia Quimica, Universidad de Chile. Biblioteca digital de la Universidad de Chile. Disponible en.
10. Damascos MA, Arribere M, Svriz M, Bran D (2008) Fruit mineral contents of six wild species of the North Andean Patagonia, Argentina. Biol Trace Elem Res 125: 72-80.
11. Suwalsky M, Vargas P, Avello M, Villena F, Sotomayor CP (2008) Human erythrocytes are affected in vitro by flavonoids of Aristotelia chilensis (Maqui) leaves. Int J Pharm 363: 85-90.
12. Munoz O, Christen P, Cretton S, Backhouse N, Torres V, et al. (2011) Chemical study and anti-inflammatory, analgesic and antioxidant activities of the leaves of Aristotelia chilensis (Mol.) Stuntz, Elaeocarpaceae. J Pharm Pharmacol 63: 849-859.
13. Escribano-Bailon MT, Alcalde-Eon C, Munoz O, Rivas-Gonzalo JC, Santos-Buelga C (2006) Anthocyanins in berries of Maqui (Aristotelia chilensis (Mol.) Stuntz). Phytochem Anal 17: 8-14.
14. Cespedes C, Alarcon J, Avila J, Nieto A (2010) Anti-inflammatory Activity of Aristotelia chilensis Mol. (Stuntz) (Elaeocarpaceae). BLACPMA 9: 127-135.
15. Cespedes C, Valdes-Morales M, Avila JG, El-Hafidi M, Alarcon J et al. (2011) Phytochemical profile and the antioxidant activity of Chilean wild black Berry fruits, Aristotelia chilensis (Mol) Stunz (Elaeocarpaceae). Food Chemistry 119: 886-895.
16. Cespedes C, Jakupovic J, Silva M, Watson W (1990) Indole alkaloids from Aristotelia chilensis. Phytochemistry 29: 1354-1356.
17. Bittner M, Silva M, Gopalakrishna E, Watson W, Zabel V. et al. (1978) New

alkaloids from Aristotelia chilensis (Mol) Stunz. J Chem Soc Chem Commun 79-80.

18. He K, Valvic S, Timmermann B, Montenegro G (1997) Indole Alkaloids from Aristotelia chilensis (Mol.) Stunz. Pharmaceutical Biology 35: 215-217.
19. Ruiz A, Hermosin-Gutierrez I, Mardones C, Vergara C, Herlitz E, et al. (2010) Polyphenols and antioxidant activity of calafate (Berberis microphylla) fruits and other native berries from Southern Chile. J Agric Food Chem 58: 6081-6089.
20. Speiski H, Lopez Alarcon C, Gomez M, Fuentes J, Sandoval Acuna C (2012) First Web-Based Database on Total Polyphenolics and Oxygen Radical Absorbance Capacity (ORAC) of fruits Produced and Consumed within the South Andes Region of South America. J Agric Food Chem 60: 8851-8859.
21. Miranda S, Aspillaga A, Perez D, Vasquez L, Martinez A, et al. (2002) Juice and phenolic fractions of the berry Aristotelia chilensis Inhibit LDL oxidation in vitro and protect human endothelial cells against oxidative stress. J Agric. Food Chem 50: 7542-7547.
22. Girones-Vilaplana A, Valentao P, Moreno DA, Ferreres F, Garcia-Viguera C, et al. (2012) New beverages of lemon juice enriched with the exotic berries maqui, acai, and blackthorn: bioactive components and in vitro biological properties. J Agric Food Chem 60: 6571-6580.
23. Girones-Vilaplana A, Villano D, Moreno DA, Garcia-Viguera C (2013) New isotonic drinks with antioxidant and biological capacities from berries (maqui, acai and blackthorn) and lemon juice. Int J Food Sci Nutr 64: 897-906.
24. Rubilar M, Jara C, Poo Y, Acevedo F, Gutierrez C, et al. (2011) Extracts of Maqui (Aristotelia chilensis) and Murta (Ugni molinae Turcz.): sources of antioxidant compounds and alfa-Glucosidase/alfa Amylase inhibitors. J Agric Food Chem 59: 1630-1637.
25. Schreckinger M, Lila A, Yousef G, De Mejia E (2012) Inhibition of alfa-Glucosidase and alfa-Amilase by Vaccinium floribundumand Aristotelia chilensis Proanthocyanidins. Chapter 6: 71-82 In: Hispanic Foods: Chemistry and Bioactive Compounds. ACS Symposium Series Vol. 1109, American Chemical Society.
26. Rojo L, Ribnicky D, Logendra S, Poulev A, Rojas-Silva P, et al. (2012) *In vitro* and in vivo anti-diabetic effects of anthocyanins from Maqui Berry (Aristotelia chilensis). Food Chemistry 13: 387-396.
27. Cespedes C, El-Hafidi M, Pavon N, Alarcon J (2008) Antioxidant and cardioprotective activities of phenolic extracts from fruits of Chilean blackberry Aristotelia chilensis (Elaeocarpaceae). Food Chemistry 107: 820-829.
28. Farias M (2009) Determinacion de los mecanismos involucrados en la actividad analgesica de las hojas de Aristotelia chilensis en un modelo de dolor termico agudo, Universidad de Chile. Facultad de Ciencias Quimicas y Farmaceuticas, Tesis para optar al Titulo de Quimico Farmaceutico.
29. Leal M (2009) Evaluacion del efecto antiinflamatorio de un concentrado de frutos de Aristotelia chilensis en un modelo de inflamacion aguda subplantar inducida por carragenina en ratas. Universidad Austral de Chile. Memoria para optar al Titulo de Medico Veterinario, Valdivia Chile.
30. Torres V (2010) Evaluacion de las actividades analgesicas, antiinflamatorias, antioxidantes y antimicrobianas de las hojas de Aristotelia chilensis y de sus potenciales efectos toxicos. Santiago. Universidad de Chile.
31. Boivin D, Blanchette M, Barrette S, Moghrabi A, Beliveau R (2007) Inhibition of cancer cell proliferation and suppression of TNF-induced activation of NFkappaB by edible berry juice. Anticancer Res 27: 937-948.
32. Youdim KA, McDonald J, Kalt W, Joseph JA (2002) Potential role of dietary flavonoids in reducing microvascular endothelium vulnerability to oxidative and inflammatory insults (small star, filled). J Nutr Biochem 13: 282-288.
33. Atalay M, Gordillo G, Roy S, Rovin B, Bagchi D, et al. (2003) Anti-angiogenic property of edible berry in a model of hemangioma. FEBS Lett 544: 252-257.
34. Arellano J, Saavedra T (2010) Berries, una nueva alternativa terapeutica en Dermatologia. Dermatol Argent 16: 212-215.
35. Ward PA, Lentsch AB (2002) Endogenous regulation of the acute inflammatory response. Mol Cell Biochem 234-235: 225-8.
36. Ojeda J, Jara E, Molina L, Parada F, Burgos R, et al. (2011) Effects of Aristotelia chilensis berry juice on cyclooxygenase 2 expression, NF-kB, NFAT, ERK1/2 and PI3K/Akt activation in colon cancer cells. BLACPMA 10: 543-552.
37. Fuentealba J, Dibarrart A, Saez-Orellana F, Fuentes-Fuentes MC, Oyanedel CN, et al. (2012) Synaptic silencing and plasma membrane dyshomeostasis induced by amyloid-B peptide are prevented by Aristotelia chilensis enriched extract. J Alzheimers Dis 31: 879-889.
38. Schreckinger ME, Lotton J, Lila MA, de Mejia EG (2010) Berries from South America: a comprehensive review on chemistry, health potential, and commercialization. J Med Food 13: 233-246.
39. Reyes-Farias M, Vasquez K, Ovalle-Marin A, Fuentes F, Parra C, et al. (2015) Chilean native fruit extracts inhibit inflammation linked to the pathogenic interaction between adipocytes and macrophages. J Med Food 18: 601-608.
40. Araneda X, Quilaman E, Martinez M, Morales D (2014) Elaboracion y evaluacion de jugo de maqui (Aristotelia chilensis (Mol.) Stunz) por arrastre de vapor. Scientia Agropecuaria 5: 149-156.
41. Brauch JE, Buchweitz M, Schweiggert RM, Carle R (2016) Detailed analyses of fresh and dried maqui (Aristotelia chilensis (Mol.) Stuntz) berries and juice. Food Chem 190: 308-316.
42. Salinas J (2012) Monografia de Maqui Aristotelia chilensis (Mol,) Stuntz. Programa de Investigacion de productos forestales no madereros. Instituto Forestal.
43. Fredes C, Montenegro G (2011) Maqui: el super fruto chileno. Rev. de Agronomia y Forestal 43: 18-20.
44. Ramirez M, Geracitano L, Marti D, Henriques A (2009) Efectos beneficiosos de extractos de frutas rojas y de sus antocianos. BLACPMA 8: 456-468.
45. Quinones M, Miguel M, Aleixandre A (2012) The polyphenols, naturally occurring compounds with beneficial effects on cardiovascular disease. Nutr Hosp 27: 76-89.
46. Miranda-Rottmann M, Aspillaga A, Perez D, Vasquez L, Martinez A et al. (2002) Juice and phenolic fractions of the Berry Aristotelia chilensis inhibit LDL oxidation in vitro and protect human endothelial cells against oxidative stress. J of Agricultural and Food Chemistry 50: 7542-7547.
47. Tanaka J, Kadekaru T, Ogawa K, Hitoe S, Shimoda H, et al. (2013) Maqui Berry (Aristotelia chilensis) and the constituent delphinidin glycoside inhibit photoreceptor cell death induced by visible light. Food Chemistry 139: 129-137.