ANTIOXIDANT ACTIVITY AND PHYTOACTIVE COMPOUNDS RELATED TO BIOLOGICAL EFFECTS PRESENT IN NATIVE SOUTHERN CHILEAN PLANTS: A REVIEW

SUSANA ALFARO ARAYA [1], AND RAMIRO DÍAZ [2]*

[1]*Facultad de Ciencias de la salud, Universidad Adventista de Chile, Camino a Tanilvoro Km. 12, Las Mariposas, Chillán, Chile.*
[2] *Facultad de Recursos Naturales, Departamento de Ciencias Biológicas y Químicas, Universidad Católica de Temuco, Rudecindo Ortega 02950, Temuco, Chile.*

ABSTRACT

Studies carried out in different native Chilean plants demonstrate that compounds found in both fruits and leaves have the capacity to decrease oxidative cellular damage in humans, thus contributing to the prevention of chronic illnesses such as diabetes, cancer, and arterial hypertension. Information on native Chilean medicinal plants was extracted from the Scopus, Science Direct, Google Scholar, and PubMed databases. Plants with relevant antioxidant activity were selected based on their chemical compounds and their use as native-flora research materials in Chile. Provitamin A, carotenoids and vitamins C and E are the main compounds found in the studied species. Several analyses also show the presence of polyphenolic and alkaloid compounds with proven capacity to increase antioxidant activity. Therefore, such native species should be of interest for the food, cosmetic, and pharmaceutical industries, as safer natural antioxidant compounds are crucial for the prevention of human illnesses and for replacing the synthetic antioxidants currently in use (BHT, BHA).

The present review aims to provide up-to-date information on the traditional uses of native plants in popular medicine, and to present evidence concerning the antioxidant activity of the studied plant species and their relationship with the active principles found.

Keywords: Antioxidant Activity, Polyphenols, Free Radicals, Native Chilean Medicinal Plants.

1. INTRODUCTION

Plants have been used for medicinal purposes throughout history, and have contributed to the development of modern pharmacotherapy. However, despite being a potential source of drugs, only a small proportion of species have been studied in relation to their chemical composition and biological activity [1].

The native Chilean flora is rich in botanical genera and species, and because of the geographical isolation of the country, it preserves specific characteristics with little genetic variability that is relatively unknown in other parts of the world [2]. Indigenous people in Chile have learned to use a myriad of medicinal plant species as part of their knowledge that is inherited after generations in contact with the natural flora. Various medicinal plants have been included as part of foreign pharmacopoeias, such as *Peumus boldus* Mol (Boldo) [3]. However, the medicinal understanding of a number of native species remains unclear and/or under-researched. For this reason, more thorough scientific studies might contribute to the use and application of natural compounds in the pharmaceutical and cosmetic industries.

According to Vogel et al [2], an in-depth chemical study of native Chilean plant species could promote therapeutic uses and encourage the cultivation of plants, thus improving the conservation and quality of the selected genetic material.

The global market has shown an increased interest in medicinal plants and their products owing to various factors, such as greater research on the pharmacological properties of traditionally used plants and herbs. The use of medicinal plants has also expanded to the food industry [4], resulting on the one hand in enhanced production and on the other in a growing consumption of nutraceuticals, as well as developments in the phytocosmetic industry [5].

Various medicinal properties have been reported for native Chilean plants. Among these, the antioxidant activity has been considered relevant in *Peumus boldus* Mol (boldo), *Haplopappus baylahuen* Remy (bailahuén), *Buddleja globosa* Hope (matico), *Fragaria chiloensis* ssp. chiloensis (Chilean wild strawberry), *Aristotelia chilensis* (Mol) Stuntz (maqui), *Ugni molinae* Turcz (murtilla), *Berberis microphyla* G. Forst (calafate) and *Berberis darwinii* (michay) (Figure 1). In the case of *P. boldus*, its antioxidant properties have been associated mainly with the presence of boldine, catechin and several phenolic compounds with known antioxidant activity [3], [6], [7], [8]. In bailahuén, terpenes, flavonoids and coumarins provide the antioxidant activity, whilst in matico, this property is primarily due to flavonoids and phenylethanoids, but also to the presence of verbascoside [2], [9], [10], [11]. The antioxidant capacity of the Chilean wild strawberry, maqui and murtilla is largely attributed to polyphenolic compounds and triterpenoids [12], [13], [14], [15], [16], [17]. In 20 species of the *Berberidaceae* family described in Chile, *B. microphyla* G. Forst shows high anthocyanin, hydroxycinnamic acid, quercetin and isorhamnetin contents, but also the presence of the alkaloid berberine [18]. In *B. darwinii* (michay), several alkaloids (particularly berberine) have also been reported in the fruits [19].

Herbal infusions and teas are vital sources of antioxidants and can be considered a complement to antioxidant intake in the human diet. The evaluation of their antioxidant activity has been carried out via the ORAC method using fluorescein and pyrogallol red as target molecules. Among six herbal teas [*H. baylahuen* Remy (bailahuen), *P. boldus*, Mol (boldo), *Matricaria chamomilla* L. (chamomile), *B. globosa,* Hope (matico), *A. citriodora* Ort (cedrón), and *C. ambrosioides* L. (paico)], the highest ORAC-fluorescein value was obtained for *A. citriodora* extracts (3368 ± 107), and the lowest in *C. ambrosoides* (395 ± 13). The order of ORAC-fluorescein values was: *A. citriodora* > *P. boldus* > *H. baylahuen* > *B. globosa* >*M. chamomilla* > *C. ambrosoides*, although when ORAC-pyrogallol red was used, the order was: *P. boldus* > *H. baylahuen* >*A. citriodora* > *B. globosa* >*M. chamomilla* > *C. ambrosoides* [9].

Nevertheless, previous studies provide valuable background information regarding the main compounds responsible for antioxidant activity and other therapeutic properties of a number of native Chilean plants and support their utilization in traditional medicine.

2. ISOLATED POLYPHENOLIC COMPOUNDS AND ANTIOXIDANT ACTIVITY

Polyphenols are by-products of plant secondary metabolism. The term "phenolic compound" includes a specific group of substances with an aromatic ring with more than one hydroxyl substituent. The structure of the natural polyphenols varies from a simple structure of molecules (like phenolic acids), to a highly polymerized compound (such as condensed tannins) (Table 1) [20], [21].

Flavonoids form part of a long list of compounds that are broadly distributed in a variety of plants and vegetables, thus forming an essential component of the human diet. Diets rich in fruits and vegetables (such as the Vegetarian and Mediterranean diets), contain a large quantity of polyphenols, and their consumption is considered healthy due to the inverse relationship found between the high intake of these compounds and the low incidence of degenerative chronic illnesses, such as cardiovascular diseases [22], [23].

Flavonoids represent the most common and most extensive group of phenolic compounds found in plants. Their common structure is (C6-C3-C6) (Figure 2), consisting of two bonded aromatic rings linked to three carbon atoms usually forming a hydrogen heterocycle [20]. The structural variation inside the ring subdivides flavonoids into several families: flavonols, flavones, flavanols, isoflavones, anthocyanins and others. These flavonoids are commonly present as

**Corresponding author email: susanaalfaro@unach.cl*

glycosides. Glycosylation improves their solubility in water and makes them less reactive to free radicals. The most common sugar involved in the formation of glycosides is glucose, although galactose, rhamnose, xylose, and arabinose are also possible, as well as rutinose, a disaccharide [1]. Other modifications are likely to occur in several stages, such as an alteration in the extension of hydroxylation, methylation, isoprenylation, dimerization and glycosylation (producing O or C glycosides). The variations of flavonoids are all related to a common biosynthetic step, incorporating precursors via the shikimate and acetate-mevalonate routes [24]. Indeed, phenolic compounds originate mainly through two biosynthetic pathways: (a) the shikímic acid route that via the synthesis of aromatic amino acids (phenylalanine, tyrosine) leads to the synthesis of cinnamic acids and their derivatives (simple phenols, phenolic and derivative acids, coumarins, lignanes and those derived from the phenyl propane), and (b) the polyacetate route, from which quinones, xanthones, dihydroxytoluene, etc., are originated. Similarly, a number of phenolic compounds, considered active principles in medicinal plants, originate from a combination of both the shikimate and acetate routes. Flavonoids and terpenic compounds arise through the combination of both mevalonate and shikimate routes (furan and pyranocoumarins, etc) [20].

Table 1. Main types of phenolic compounds present in plants

Number of Carbon atoms	Basic skeleton	Polyphenol class	Polyphenol compound
6	C6	Simple phenols Benzoquinones	Catechol, hydroquinone 2,6-Dimethoxybenzoquinone
7	C6-C1	Phenolic acid	Gallic, salicylic
8	C6-C2	Acetophenones Tyrosine derivatives Phenylacetic acid	3-Acetyl-6-methoxybenzaldehyde Tyrosol p-Hydroxyphenylacetic
9	C6-C3	Hydrocinnamic acid Phenylpropene Coumarin Isocoumarin Chromones	Caffeic, ferulic Myristicin, eugenol Umbelliferone, aesculetin Bergenon Eugenin
10	C6-C4	Naphthoquinones	Juglone, plumbagin
13	C6-C1-C6	Xanthones	Mangiferin
14	C6-C2-C6	Stilbenes Anthraquinones	Resveratrol Emodin
15	C6-C3-C6	Flavonoids Isoflavonoids	Quercetin, cyanidin Genistein
18	(C6-C3)2	Lignans Neolignans	Pinoresinol Eusiderin
30	(C6-C3-C6)2	Biflavonoids	Amentoflavone
n	(C6-C3)n (C6)n (C6-C3-C6)n	Lignins Catechol melanins Flavolanas (condensed tannins)	

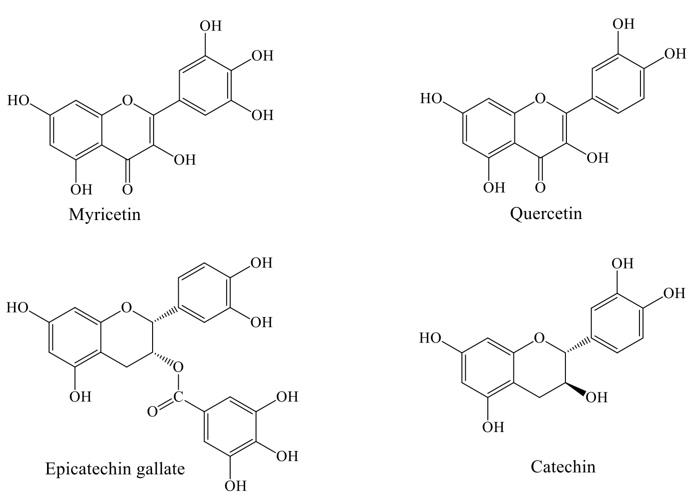

Figure 2. Basic structure of flavonoids (C6-C3-C6)

3. Biological effects of polyphenols

Polyphenols exhibit a wide range of biological effects due to their antioxidant properties. They inhibit *in vitro* oxidation of LDL and may provide protection to oxidation, with significant consequences in the treatment of atherosclerosis [15], [25].

Phenolic compounds act as antioxidants with mechanisms such as free radical scavenging and chelation of metals. They have an ideal chemical structure for trapping free radicals, and on a molar basis, show a more effective *in vitro* antioxidant effect than that of vitamins C and E [23].

In contrast, due to protection against oxidative DNA damage, these compounds might also prove crucial in the development and progression of cancers [26], [27]. Indeed, several polyphenol types (phenolic acids, hydrolysable tannins and flavonoids) show anticancer and antimutagenic properties. Polyphenols interfere in several of the steps leading towards the development of malignant tumors by inactivating carcinogens and inhibiting the expression of mutant genes. Additionally, polyphenols can hinder the activity of enzymes involved in the activation of procarcinogens and inhibit enzymatic systems required for the detoxification of xenobiotics. Hence consumption of high-phenolic fruits, such as strawberries and blackberry may help in the prevention of some types of cancer such as colorectal cancer [22].

Wine contains compounds that appear to exhibit anticancer properties, including gallic, caffeic and ferulic acids, as well as catechins, meletins and resveratrol (Figure 3). Flavonoids possess antithrombotic and anti-inflammatory properties [23]. Studies have shown that these compounds are positive for the prevention of urinary tract illnesses by impeding the adhesion of uropathogen microorganisms to the epithelial mucosa [28], [29], [30].

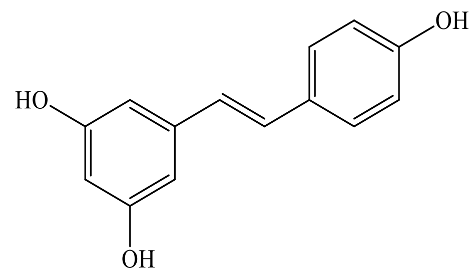

Figure 3. Resveratrol (stilbene)

However, the bioavailability of food polyphenols varies depending on the type of metabolite, and most polyphenols are largely metabolized by the gut microorganisms before being absorbed. In addition, technological processes and consumer habits considerably affect the bioavailability and bioactivity of the antioxidant metabolites ingested [31]. Several studies have found that these compounds may be affected by factors, such as plant variety, growing environment, growing season, climate, temperature, light, soil type and other conditions (such as processing and post-harvest storage), all of which may affect both antioxidant content and antioxidant activity [32], [33].

A study in murtilla fruit, developed by INIA-Chile, found that the qualitative and quantitative composition of phenolic compounds in fruits is unique to individual species and genotypes. A canonical discriminant analysis of seasonal differences in the Red Pearl-INIA, South Pearl-INIA and 14-4 genotypes showed that the South Pearl-INIA variety suffers the largest variation in comparison to the other genotypes. On the other hand, large differences in total polyphenol content were observed between harvest years, partly due to variations in weather conditions across the growing seasons, as well as differences in rainfall and/or number of frosts [34].

4. Native plants as significant sources of natural antioxidants

On an ethno-cultural basis, the Mapuche medicinal flora is based on a deep, extensive and diverse knowledge of the sources of natural antioxidants in different varieties of local plants. In fact, it is possible to establish a classification system of medicinal plants based on their organoleptic characteristics and potential health benefits. Additionally, the cultural interpretations of flavor and aroma are key features for accurately determining the active principles likely to be found in plants. These organoleptic characteristics usually come from secondary metabolites in plant tissues, such as terpenoids and derivates [35], [36], tannins or other components [37].

The use of medicinal plants is still an essential aspect of the Mapuche people, connecting the different natural plant properties with a specific symbolic conception of the natural world. Nowadays, however, knowledge regarding horticultural practices of medicinal plants is significantly less. The use of native Chilean medicinal flora is a key aspect in terms of recognizing species richness, diversity and biogeographic origins. Among these, *Chenopodium* spp. (*Chenopodiaceae*), *A.chilensis* and *L. apiculata* (DC) Burret (*Myrtaceae*), were the most significant. Given the fact that the presence of active secondary metabolites is a crucial characteristic of medicinal plants, it is not surprising that this feature is found in a large number of species with noteworthy pharmacological and organoleptic properties. Similar properties have also been found in other native species, such as *B. globosa* Hope (*Buddlejaceae*). In particular, the anti-inflammatory and antioxidant uses of *B. globosa* have been studied by Backhouse et al [10]. Various reports have linked the anti-diabetic effects of plants to the presence of phenolic compounds found in the fruits (maqui), thus establishing a correlation with their antioxidant capacity and anti-diabesity activities (lipase and a-glucosidase inhibition) [38], [39].

Table 2. Summary of compounds with antioxidant properties found in native Chilean plants

Common name	Scientific name	Species	Part used	Isolated polyphenolic compounds	Method used	Reference
Frutilla chilena, frutilla patagónica	*Fragaria chiloensis, Fragaria patagónica*	*Fragaria chiloensis* ssp. *chiloensis*	Achenes (real fruit) and thalamus (receptacle)	Flavonoids Anthocyanins: Cyanidin derivatives. Pelargonidin derivatives and Petunidin or malvidin derivatives	Spectrophotometry (DPPH), total phenols by Folin-Ciocalteau, total anthocyanins by differential method of pH HPLC	[40]
Frutilla chilena, frutilla patagónica	*Fragaria chiloensis, Fragaria patagónica*	*Fragaria chiloensis* ssp. *chiloensis*	Fruits	Proanthocyanidins, hydrolysable tannins, flavonol glycosides: quercetin 3-O-glucuronide; anthocyanins: cyanidin-malonyl-glucoside and pelargonidin-malonyl- glucoside	HPLC–DAD HPLC–ESI–MS	[41]
Bailahuén	*Haplopappus bailahuen* *H. remyanis* *H. taeda*	*Haplopappus* ssp	Leaves	Terpenes, flavonoids, cumarins (prenyletin), monoterpene (taedol), diterpenoids	Lipid Peroxidation in erythrocyte membrane, DPPH ORAC ^{1}H-,^{13}C-NMR and mass spectrometry	[2] [42] [43] [44], [45]
Boldo	*Peumus boldus*	*Peumus boldus* Mol**.**	Leaves	Flavonoids: catechine, epicatechine, gallic acid, tamic acid, tannins, alkaloid aporphines: boldine Essential oils: Ascaridol, cineol	TBARS O_2 Uptake	[2] [8] [46] [47] [48] [49] [50] [51]
Boldo	*Peumus boldus*	*Peumus boldus* Mol**.**	Fruit	catechin, epicatechine	HPLC-DAD, HPLC-MS / MS	[52] [53]
Maqui	*Aristotelia chilensis*	*Aristotelia chilensis* (Mol.) Stuntz	Fruit	Anthocyanins (delphinidin, cyanidin, delphinidin-3-3-sambubiosido-5-glucoside	HPLC–coupled PAD and MAS HPTLC	[54] [55] [56] [57] [58] [59], [4], [58] [60]
Murtilla	*Ugni molinae* Turcz	*Ugni molinae* Turcz	Leaves	Flavonols, flavanols myricetin and quercetin glycosides Epicatechines gallic acid	DPPH TBARS HPLC-MS	[61] [62] [16] [63]
Murtilla	*Ugni molinae* Turcz	*Ugni molinae* Turcz	Fruits	Flavonols glycosides : Myricetin glucoside, quercetin glucoside, quercetin glucuronide and quercetin dirhamnoside	HPLC–DAD–MS HPLC UV-vis DPPH assay TEAC assay ITC (Folin Ciocalteu)	[64] [65] [62] [34], [66] [67]
Murtilla	*Ugni molinae* Turcz	*Ugni molinae* Turcz	Leaves	Flavonoid glycosides of quercetine, myricetin and kaempferol Triterpenoids (asiatic, corosolic, alphitolic, botulinic, oleanolic and ursolic acid)	Chromatographic method (TLC, HPLC) by NMR. Acute pain models in mice (writhing test, tail flick assay and tail formalin test)	[12] [68]
Murtilla	*Ugni molinae* Turcz	*Ugni molinae* Turcz	Leaves	Phenols, flavonoids and tannins (catechin, epicatechine, myricetin)	Scanning electron microscope (SEM) studies of human erythrocytes. Fluorescence measurement of isolated human erythrocytes membranes (IUM) and DMPC of large unilamellar vesicles (LUV)	[69]
Matico	*Buddleja globosa*	*Buddlejaceae*	Leaves	Pentacyclic triterpenoids (β and α amyrin) sterols, β sitosterol glucoside, ergosterol, stigmasterol) phenylethanoids, flavonols, verbascoside, luteolin glucoside	Chromatographic methods (TLC, HPLC-DAD, GS-MS) y ^{1}H y ^{13}C NMR. DPPH IC_{50} % XO inh. % SO inh. % L Perox inh. Acute pain models in mice (writhing test, tail flick assay and tail formalin test; wound-healing bioassays	[70] [71] [72] [73] [74]
Calafate Michay	*B. microphylla G.* Forst *B. darwinii* *B. empetrifolia* *B. ilicifolia* *B. montana*	*Berberidaceae*	Fruits Seeds Roots Stems Leaves	Hydroxycinnamic acid Anthocyanins Flavonols Flavan 3-ols Alkaloids	HPLC-DAD-ESI-MS/ MS and HPLC with fluorescence detection UV-vis NMR spectroscopies TEAC assay Folin Ciocalteu (IFC)	[75] [76] [18] [77] [78] [79] [80]

4.1. *Peumus boldus* Mol. (boldo)

P. boldus leaves (boldo) are traditionally used in folk medicine and are now widely recognized as a herbal medicine in many pharmacopoeias. *P. boldus* is an abundant native tree from south-central Chile, although it can be found from Fray Jorge, IV Region (Coquimbo) in the north, to the X Region (Los Lagos) in the south, where it grows mainly in the lower sunny slopes of both the Andes and the Coastal Mountain ranges, but also in the Central Valley [3], [81]. Its leaves are rich in various kinds of aporphine alkaloids. They contain between 0.4 and 0.5% of more than 17 different alkaloids found in the large family of benzylisoquinoline derivatives. Among the alkaloids, boldine (2,9-dihydroxy-1,10-dimethoxyaporphine) (Figure 4) is one of the most abundant in *P. boldus* leaves representing between 12 to 19% of the total content of these compounds [82]. Based on mechanisms linking structure with the capacity to react with free radicals, boldine is considered one of the most potent natural antioxidants [1], [8], [83], [84].

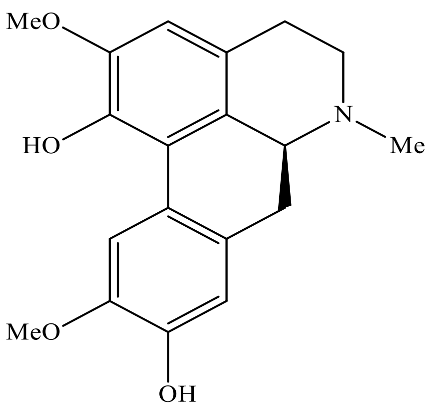

Figure 4. Boldine structure

P. boldus leaves also contain 1.2% tannins, 2-3% essential oils (up to 45% ascaridol and 30% cineole and at least 22 other identified constituents, mostly terpenoids) [3], and flavonoids, including catechin and rutin [85]. This latter component has recently been reported in *P. boldus* fruits, as being among the most abundant [52]. The content of catechins, gallic acid and tannic acid is higher than that of boldine. These compounds appear to make the greatest contribution towards the total antioxidant activity of *P. boldus* infusions [8]. In this context, infusions of this plant species act as a protector against the oxidative damage caused by cisplatin in the liver tissue due to the presence of boldine, suggesting the potential use of the infusion as a chemoprotector [51].

The phenolic hydroxyl groups of boldine contribute to its antioxidant nature. Low boldine concentrations ($IC_{50} = 5 \times 10^{-6}$ to 15×10^{-6} M) have a demonstrated protective effect on the plasmatic membrane of erythrocytes against the increment of reactive species induced by AAPH (2,2'-Azobis[2-amidinopropane]), which generates alkylperoxyl radicals by thermal decomposition. In such systems, the antioxidant capacity of boldine ($Ki = 13$ µM) was significant and similar to that reported for the widely used bioflavonoid (+)-cyanidanol-3. The effective inhibition of spontaneous auto-oxidation has also been proven in brain membrane lipids [carried out by the production of reactive substances of thiobarbituric acid (TBARS), O_2 uptake and chemiluminescence], with an apparent K_i of 19 - 30 µM. Studies on the mechanisms involved in the antioxidant action of boldine indicate that this alkaloid acts as an efficient scavenger of HO·. In addition, a significant correlation between activity and the protective effect in models of induced oxidative stress damage has been observed [8]. In fish oil, boldine showed a similar activity to that of quercetin and two to three times greater activity than α-tocopherol, BHA or BHT [86]. Most of these biological effects are attributable to their strong free radical scavenging ability [82], [87].

However, other studies indicate that boldine may not be the only agent responsible for antioxidant activity in *P. boldus* extracts. Simirgiotis and Schmeda-Hirschmann [6] suggest that their strong free-radical activity is mainly due to polyphenol compounds such as catechin and flavonoids rather than boldine, due to their relative concentrations in *P. boldus* extracts [88]. Also, boldine has recently been shown to harbor UV light-filtering properties and to display a photoprotector effect against UV-B [89]. It also has promising protective effects against cisplatin nephrotoxicity by improving oxidative stress, inflammation, histopathological alterations and by alleviating caspase 3 expression [47].

Extracts of *P. boldus* leaves contain a wide range of phytochemicals such as essential oils, isoprenoids, flavonoids, various alkaloids and other compounds [90]. The most favorable extraction conditions for obtaining maximum boldine yields in the first step were determined at 70°C for 6 h using stem tissues. The values of total phenolic content (hydrolysable polyphenols and condensed polyphenols) in the extracts with maximum boldine concentrations were obtained at 6 and 24 h [88]. In accordance with this study, the maximum boldine yield was found in stem tissue extracts while the maximum polyphenolic content was obtained from leaf extracts. The maximum content of boldine was also observed in extracts from the longest extraction period (24 h) and the maximum phenolic content was observed in extracts from the shortest extraction period (6 h). Therefore, these results suggest that the antioxidant activity of *P. boldus* is more related to that of other compounds such as the polyphenols, instead of boldine. Most of the total polyphenolic content was in the form of polyphenols from the condensed group, such as catechin and flavonoids, which were reported in *P. boldus* extracts by Simirgiotis and Schmeda-Hirschmann [6]. However, the defensive capability of *P. boldus* extracts could be due to the existence of natural antioxidants and anti-inflammatory constituents, such as gallic acid, ellagic acid, querectin, daidzein, ferulic acid and rutin [84].

4.2. *Haplopappus baylahuen* Remy (bailahuén)

The natural habitat of this species (*H. baylahuen* Remy) is limited to the Chilean mountain areas between latitudes 26 and 28ºS. Nonetheless, in other regions of Chile, other endemic *Haplopappus* species, such as *H. multifolius* Phil. (32-34ºS), *H. remyanus* Reiche (29-32ºS) and *H. taeda* Wedd (34-35ºS) can also be found, sold and/or exported. The flavonoid and coumarin contents of these four species have been established, and most compounds in *H. baylahuen* are terpenes, flavonoids and coumarins such as prenyletin [2], [43], [91].

The antioxidant evaluations of aqueous extracts of *H. baylahuen* show that they have similar concentrations of catechins and are three times more potent than aqueous extracts of *P. boldus* (boldo) in the inhibition of lipid peroxidation. The other *Haplopappus* species studied showed significantly higher antioxidant properties, similar to those found in *H. baylahuen*, with differences in chemical composition, including a prevalence of flavonoids in *H. taeda*, coumarins in *H. multifolius*, and both substances in *H. remyanus* and *H. baylahuen*. The total phenol content (expressed as mg Gallic acid equivalent/L) in herbal infusions was highest in *P. boldus* (376±4) compared to > *H. baylahuen* (245±11) > *Buddleja globosa* (165±5), all of which are lower total phenol content than that found in black tea samples (677±16). The same order was observed in the three native Chilean species when using the ORAC methodology [9].

Studies on the relationship between antioxidant efficiency and hepatoprotective effects confirm the effectiveness of popular applications of *H. multifolius* and *H. taeda* in Chile. The antioxidant efficiency of *H. remyanus* (such as bailahuen) has been described to be five times that of *H. baylahuen*, mainly due to the higher content of polyphenolic compounds [2]. Differences in the main constituents of infusion and methanolic extracts of the various *Haplopappus* species commercialized as "bailahuen" tea in Chile have been found in a study by Schmeda-Hirschmann et al [91] using HPLC-DAD-ESI-MS. This method was developed for the fast identification and differentiation of *Haplopappus* spp. used as a tea source, based on the phenolics found in tea and methanol extracts. Twenty-seven phenolics were tentatively identified in the infusions and methanol extracts, including 10 caffeoyl quinic and feruloyl quinic acid derivatives and 17 flavonoids [92].

The antioxidant effect of the extracts was determined by the DPPH assay, indicating that *H. multifolius* and *H. taeda* are the best source of free radical scavengers. This trend is in agreement with the total phenolic and flavonoid content of the samples [91].

In contrast, Torres et al., (2004) reported two new coumarins isolated from the resinous leaf exudates of *H. multifolius* (Figure 5), and designated the structures as 6-hydroxy-7-(5'-hydroxy-3',7'-dimethylocta-2',6'-dien)-oxycoumarin (1), and 6-hydroxy-7-(7'-hydroxy-3',7'-dimethylocta-2',5'-dien)-oxycoumarin (2).

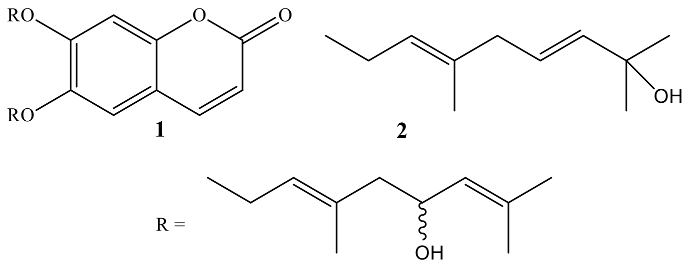

Figure 5. Structure of coumarins 1 y 2 of H. multifolius leaves

Faini et al [44], reported two new phenolic esters from *H. taeda* resinous exudate from aerial parts; 9-*trans*-p-coumaroyloxy-α-terpineol (1), and 7-*trans*-p-coumaroyloxy-taedol (2), both endowed with free radical scavenging activity (Figure 6).

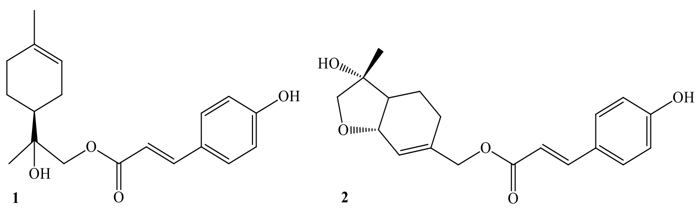

Figure 6. Phenolic esters 1 and 2, isolated from the resinous exudates of H. taeda.

In other studies, Faini et al [45] reported that the terpenoid-rich *H. baylahuen*, showed the lowest antioxidant activity, whilst the higher activities of extracts from other *Haplopappus* species could be attributed to the presence of coumarins (*H. multifolius*) and flavonoids (*H. taeda* and *H. remyanus*). The authors isolated three dihydroflavones, two labdanoic acids and six monoterpene esters. *H. remyanus* produces 7-O-methyl-flavonoids and characteristic 9-hydroxy α-terpineol esters, thus differentiating it from other "bailahuen" species that accumulate coumarins and/or diterpenoids. The presence of flavonones in *H. remyanus* had previously been reported by Zdero at al [93]. Variations in chemical composition and bioactivity within individuals of the same species are not uncommon, as the production of secondary metabolites in plants is closely associated to the predominant environmental conditions of the habitat [66], [94].

Results of *H. remyanus* anti-inflammatory, antioxidant and cytotoxic extract bioassays show moderate -but relevant- activities due mainly to the presence of flavonoids [45]. Hydroxycinnamic acid derivatives and flavonoids could explain the reputed nutraceutical and health beneficial properties of this herbal tea [91].

4.3. *Buddleja globosa* Hope (Matico)

This Chilean species is distributed in hills and gulches, alongside roads and heaths, between Santiago and Chiloé, although scarce in the central region and more frequent in the south of the country. It is a bush of 2.5 to 3 m in height, composed of simple opposite leaves, 10 to 15 cm long, oval–lanceolate in shape, rough and porous in surface and covered with abundant filaments that give it a greyish aspect. Leaves and flowers are utilized in popular medicine for the treatment of wounds, ulcers and intestinal affections. The leaves are also used for dyeing textiles brown [81].

A mixture of known triterpenes and steroids have been isolated and identified from the active fractions of *B. globosa*. Recent studies describe triterpenes, diterpenes, phenylethanoids and flavonoids as the main constituents [70], [95], [96]. Therapeutic analgesic and anti-inflammatory healing effects have been reported in hydro alcoholic extracts of shoots and in dichloromethane extracts of roots [10]. The antinociceptive effects of a mixture of α and β-amyrin have recently been demonstrated in several *in vivo* models. A mixture of amyrin (43, 7%), β-amyrin (24, 9%) and bauerenol (31, 4%) showed a higher analgesic effect (51%) than the anti-inflammatory activity (20%) [11]. A total of 17 compounds were identified in *B. globosa* extracts, spanning 13 phenylpropanoids and 4 flavonoid glycosides. To the best of our knowledge, caffeoylglucoside isomers, caffeoylshikimic acid, β-hydroxy-verbascoside, β-hydroxyisoverbascoside, quercetin-3-O-glucoside, campneoside I, forsythoside B, lipedoside A, forsythoside A, eukovoside and martynoside were identified for the first time using liquid chromatography coupled with IT and TOF [70].

The effect of a similar mixture of α and β−amyrin has been related to a stabilizing action on mast cell membranes involved in the inflammation process. A dose-dependent topical anti-inflammatory effect of stigmasterol and β−sistorerol in TPA models was accompanied by lower myeloperoxidase activity. A marked influence on the inhibition of neutrophil migration into inflamed tissue has also been described [73].

The anti-inflammatory, analgesic and antioxidant activities are related to the verbascoside and luteolin 7-O-glucoside contents. Luteolin glucosides exhibit a moderate inhibitory activity on both thromboxane and leukotriene synthesis and harbor anti-inflammatory and antioxidant activities [72]. The protective effect of verbascoside against plasma lipid peroxidation has been demonstrated. The high redox potentials of verbascoside protect cells against glucose oxidase-mediated cytotoxity and apoptosis. A preventive potential may be attributed to the treatment of oxidative stress-mediated illnesses. Verbascoside showed inhibitory effects of histamine, bradykinin-induced contractions and oral anti-inflammatory activity [10], [72], [97].

According to Houghton et al [98], extracts have been shown to have anti-inflammatory and antioxidant properties due to the presence of flavonoids, triterpenoids, diterpenoids and caffeic acids derivates. The extracts had polyvalent activity in the potential for healing wounds. *B. globosa* leaf extracts induced differentiation in keratinocytes and altered protein profiles produced by cultured fibroblasts. The extracts have a number of effects on lattice contraction. Recent experiments showed that under extremely low concentrations, the extracts reduced hemolysis induced by HClO (hypochlorous acid). Results demonstrated that low *B. globosa* aqueous extract concentrations neutralized the harmful effects of HClO. The phenolic acids and flavonols present in the extract are the only compounds responsible for such protective effects, as they directly interact with reactive oxygen species [99]. Other results suggest that the most abundant constituent in *B. globosa* is catechin [71].

In others studies, Letelier et al [100] compared the redox reactivity of free oxygen radicals and DPPH radicals of phospholipids and protein thiol groups present in rat liver microsomes. Cu^{2+}/ascorbate was used as a generator system of free oxygen radicals, with extracts of *B. globosa* leaves used as an antioxidant. Cu^{2+}/ascorbate provoked microsomal lipid peroxidation, microsomal thiol oxidations and oxygen consumption; all of these phenomena were inhibited by *B. globosa* extracts. These herbal extracts prevented the free oxygen radical modifications of biomolecules by similar mechanisms as those used *in vivo*, i.e. polyphenols, acting as hydrogen donors to neutralize free oxygen radicals, though not preventing nor reversing the reduction of the microsomal thiol content provoked by DPPH radicals. Studies carried out on standardized dry extracts from *Rosmarinus officinalis*, *B. globosa* Hope, *Cynara scolymus* L., *Echinacea purpurea* and *Hedera helix* were tested to evaluate their capacity to decrease drug-induced oxidative stress. Results showed that previously-evaluated antioxidant phytodrugs proved efficient in alleviating the adverse effects of drugs associated with oxidative stress [71], [101]. In more recent studies, the main polyphenols present in plant extracts of *B. globosa*, such as verbascoside and/or luteolin in aqueous solutions of silver nitrate, induce the reduction of Ag^{2+} ions into Ag^0, proving to be an efficient bioproduct to synthesize Silver nanoparticles (AgNPs) with spherical shapes [102], and in the synthesis of Zinc oxide nanoparticles (ZnONPs) [103].

4.4. *Fragaria chiloensis* ssp. *chiloensis* (Chilean wild strawberry)

The cultivated strawberry (*Fragaria ananassa* Duch. ex Rozier) originated from an accidental cross between white-fruited Chilean strawberry [*F. chiloensis* (L.) Mill. subsp. *chiloensis f. chiloensis*] and the meadow strawberry (*F. virginiana* Mill. subsp. virginiana) in the Royal Botanical Garden in France [104], [105]. *F.virginiana* is a native octoploid (2n = 8x = 56) species distributed throughout much of North America. In Chile, the native people of the Biobío region (the Picunche to the north of the Biobio river, and the Mapuche, to the south), have cultivated strawberries for over 1000 years [106]. In botanical terms, *F. chiloensis* ssp. *chiloensis* is a perennial herb, with strong and well-developed runners and trifoliate leaves with unique or few flowers, which can be dioic or hermaphrodite. The berry is an aggregate fruit, which develops from a flower that contains several ovaries.

The main studies on this fruit have been focused on the comparison of the phenolic content in achenes (true fruit) and thalamus (receptacle) utilizing the native South American species; *F. chiloensis* ssp *chiloensis* (*F. Patagónica* and *F. Chiloensis*) (with red and white fruits, respectively), *F. vesca and F. x ananassa* (cv. Chandler). The free antiradical effect has been assessed in relation to the phenolic content of these species [107], [108], [109]. In fruit extracts, 38 volatiles and 27 phenolic compounds were identified, detecting differences among the samples, which were also influenced by climatic conditions and location [110]. The total polyphenol, flavonoid and anthocyanin contents in achenes and thalamus were determined by spectrophotometric methods and compared to those of other species such as *F. vesca* and *F. ananassa* cv. Chandler. The highest polyphenol content was observed in *F. vesca* while the lowest was found in white strawberry (*F. chiloensis* ssp. *chiloensis, F. chiloensis*). Total anthocyanins and polyphenol contents were low in white strawberry and high in *F. x ananassa* cv. Chandler. Total flavonoid content showed a consistent correlation with total anthocyanins in all species, with the free radical scavenging effects of the extracts measured by the DPPH assay. Phenolic compound content differed significantly between species and sub species, and is an indication of the free antioxidant activity of the fruits [110]. The highest total anthocyanin levels were observed in the achenes of *F. chiloensis* and *F. vesca*, while the highest anthocyanin contents (95%) occurred in the thalamus of *F ananassa*, consisting mainly of derivative pelargonidin. This anthocyanin was also present in *F. chiloensis* ssp. *chiloensis F. patagonica* (62,2%) but was not detected in *F. vesca* and *F. chiloensis* ssp. *chiloensis.* Cyanidin derivatives were present in both thalamus and achenes of *F. vesca* and *F. chiloensis* ssp. *chiloensis F. chiloensis* [40], [107], [109].

Another study examined the main antioxidants from methanolic extracts of *F. chiloensis* ssp. *chiloensis F. chiloensis* (white fruits), *F chiloensis* ssp *chiloensis F. Patagonica* (red fruits) and the commercial strawberry *F. x ananassa* Duch cv. Chandler. Extract fractionation was carried out by means of the DPPH bleaching assay for isolating the dominant polyphenolic compounds present in the extracts of the berries. Phenolic compounds were compared in the three samples using both HPLC-DAD and HPLC-ESI-MS methods. All methanol extracts possessed DPPH scavenging activity and those from the red fruits of *F. x ananassa* cv. Chandler showed the highest activity (60.16 µg/ml) followed by the native red strawberry (72.32 µg/ml) and the native white strawberry (86.16 µg/ml). Furthermore, IC_{50} values for extracts of *F. chiloensis* cultivated at two different sites in Indonesia were found to be 152.9 µg/ml in the Alahan Panjang area and 232.6 µg/ml in Padang Panjang [107]. Four antioxidant compounds were isolated by Column Chromatography and High Speed Centrifugal Countercurrent Chromatography (HSCCC) from the methanolic fruit extracts of *F. chiloensis* ssp. *chiloensis* using DPPH radical scavenging as a guiding assay for selective fractionation. Although the high polarity and complexity made the isolation of the active components in the fractionation of the crude extract difficult, the use of optimized HPLC conditions coupled to diode array and mass detection favored the detection of several unreported constituents for both forms of *F. chiloensis* and proved that the white fruits of *F. chiloensis* were rich in phenolic antioxidants. Furthermore, the quantification of anthocyanins, ellagic acid and flavonols showed that there was significant variation in the phenolic antioxidant content in the methanol extract from the fruit of both *F. chiloensis* and *F. ananassa* cv Chandler. The differences found in the profiles and in anthocyanin and ellagic acid contents could underlie the variations in free radical scavenging activity of the fruits, and could also be used for chemically differentiating the commercial and the Chilean white strawberry [97], [108], [110], [111].

The relatively high antioxidant capacity, phytochemical composition and biological activity potential of these aromatic fruits mean that the Chilean white strawberry is a promising resource as a functional food and as a source of compounds with several applications in the pharmaceutical, biotechnological, and food science industries [97], [110]. Indeed, the Chilean strawberry has several known preventive and therapeutic health benefits [112]. The antioxidant content in strawberries contributes to lessening the risk of cardiovascular incidence by inhibition of LDL-cholesterol oxidation or improving vascular endothelial function. Recent studies also show a reduction in the incidence of thrombosis [14], [109]. The extracts of these fruits have crucial inhibitory-like features in the inflammatory response of the interaction between adipocytes and macrophages, acting as a potential therapeutic tool against comorbidities associated with obesity development [113]. *F. chiloensis* is a rich source of phenolic compounds and aromatic volatiles, offering a prospective alternative for the management of postprandial hyperglycemia [110]. One study showed that antioxidant activity decreases during the gastrointestinal process, constituting a first approach towards understanding the effects induced by gastrointestinal digestion on the bioactivity and polyphenolic profile of this native fruit [114].

4.5. *Aristotelia chilensis* (Mol) Stuntz (Maqui)

Aristothelia chilensis (Mol) Stuntz (Chilean maqui) is found in both the Central Valley and the Andes mountain range, between latitudes 31° and 40° (Illapel and Chiloé, respectively), although it can also be found in Juan Fernández island. *A. chilensis* grows preferably in humid areas where the soil is under permanent vegetational cover, but also on hillsides at forest margins. The fruit consists of a black, shiny berry that is 5 mm in diameter, with a sweet edible pulp. The juice of *A. chilensis* is rich in coloring agents commonly used for dyeing and staining natural materials, and for improving the color of red wines [81].

Traditional Chilean medicine attributes multiple healing properties to *A. chilensis*, with its high antioxidant potential the main benefit to human health [15], [115], [116], [117]. Other potential advantages include anti-atherogenic activities [15], prevention of visual problems [12], [118], [119], and anti-tumoral activity on a number of human leukemia and human colon carcinomas [26], [56], [120]. Several properties of *A. chilensis* have had an impact on industrial applications, such as food packaging [121]. The qualitative and quantitative analysis of *A. chilensis* leaf extracts by HPLC-DAD-ESI-MS showed the presence of different polyphenolic compounds classified into galloyl and caffeoyl quinic acids, ellagitannins and ellagic acid- and flavonoid-derivatives [122].

In addition, six alkaloids, indol and quinolines [123], [124] were described. The authors found a high polyphenolic compound content and antioxidant capacity, which protect LDLs from oxidation and endothelial cells from intracellular oxidative stress. The phenolic compound content in *A. chilensis* was compared with different commercial varieties of berries. Red wine was also included as it is a known source rich in dietary phenols. The TRAP value is a measurement that indicates free radical amounts trapped by the sample and therefore determines the presence of total antioxidants, thus correlating with total polyphenolic compound contents. TAR values indicate the capacity of the sample to decrease the stable state of the free radical concentration and are therefore considered both an accurate antioxidant quality index and an improved correlation measure between TAR and total polyphenol content [15].

In another study, it was observed that the drying process affects the content of bioactive compounds and antioxidant activity. The levels of total phenolics were found to be highest at 60 °C, while that of total flavonoids, at 70 °C [125].

The increment in retardation time of LDL oxidation is proportional to the capacity of the antioxidants to recycle the antioxidants of endogenous LDL extension. Therefore, it is a measure of the antioxidant capacity of a particular compound. It was found that the retardation time was longer with the addition of *A. chilensis* juice than with either commercial strawberry or blackberry juice. Similar protection was observed in aqueous, neutral and acid fractions, indicating a reduced improvement on the protection of intracellular oxidative stress with other phenolic compounds that are less abundant in berries [126], [127], [128].

A. chilensis has substantial levels of phenolic compounds with high antioxidant capacity which protect both LDLs from oxidation and endothelial cells from intracellular oxidative stress, suggesting the presence of antiatherogenic and cardioprotective properties in extracts of this native species [55], [59], [129], [130].

The development of techniques such as HPLC coupled to PAD and MS detection, has led to rapid advances in the identification of anthocyanin composition in many plants [131], [132]. However, the anthocyanin composition of *A. chilensis* has been scarcely studied, although a number of delphinidine, cyanidin, malvidin and petunidin mono and di-glycosides have been identified by means of TLC and spectrophotometric characteristics. Maximum peaks obtained within the visible region via modern HPLC DAD-MS techniques resulted in values of 526 and 516 nm for delphinidin-3-glucoside and cyanidin-3-glucoside, respectively, in comparison with standard anthocyanins. This was confirmed by UV-sense and MS characterization.

The nature of the sugar substituent (glucose) was confirmed by HPTLC following the isolation of compounds and acid hydrolysis [56], [60], [133], [134]. The identified pigments corresponded to delphinidin 3-diglycoside, delphinidin 3,5-diglycoside, delphinidin 3-sambubiosides and cyanidin 3-sambubiosides-5-glucoside. The main anthocyanin was delphinidin 3-sambubiosido-5-glucoside (34% of total anthocyanin content). Total anthocyanin content was 137.6 mg/100 g of fresh fruit (211.9 mg/100 g of dry fruit). The relatively high anthocyanin content and the presence of polar poliglycosylated derivatives position the fruit of *A. chilensis* as an interesting source of anthocyanin extracts for pharmaceutical and nutritional uses [56]. In other chemical composition studies of *A. chilensis* extracts, hydrophilic compounds, such as organic acids (ferulic and gallic acid), glycoside flavonoids (anthocyanidin glucosides), and hydrophobic compounds (flavonoid aglycones, such as catechins and anthocyanidins) were reported as active components from different origins [80]. Hydroxycinnamic acids were also present, although not in significant concentrations [135]. High polyphenol contents in different forms of delphinidin and cyanidin glycosides and di-glycoside were recently found in this edible fruit [38], [136].

Crude extracts of leaves and fruits of *A. chilensis* were found to be a significant source of polyphenolic compounds. Polyphenols from leaves were active as antioxidants and antihemolytic compounds, thus showing a noncompetitive inhibiting effect on α-glucosidase. Flavan-3-ol polymers and glycosylated flavonols, such as quercetin glucoside and kaempferol glucoside, were identified in extracts. This feature is key as it means that polyphenol-enriched extracts from *A. chilensis* are suitable as both nutritional and medicinal supplements with potential human health benefits [39], [137]. The conditions for antioxidant extraction are crucial for the optimizing the amounts obtained from *A. chilensis*. Recently, using a second-order polynomial model, aqueous acetone resulted to be the most effective solvent for the extraction of antioxidants from maqui berry for maximizing the ORAC value, whilst the efficiency of methanol and ethanol extracts was independent of the extraction time [138].

In spite of the demonstrated potential of *A. chilensis* as a functional ingredient, the benefits of its extract, such as the stability and variations on the polyphenol profile, and the effect of gastrointestinal digestion, remain to be fully explored. Nevertheless, recent studies have determined that all polyphenolic compounds show a decrease in concentration during *in vitro* gastrointestinal digestion. Additionally, anthocyanin contents decreased dramatically suggesting that although a large amount of polyphenols are lost during the process of digestion, they still have a high antioxidant activity [139].

The broad chemical profile of *A. chilensis* (flavonoids, anthocyanins, and phenolic acids) is directly related to its high biological potential. Our current knowledge about the antioxidant, anti-inflammatory, and hypoglycemic effects of *A. chilensis* suggests that a diet including *A. chilensis* could aid in the prevention of cardiovascular diseases. The influences of this species have been mainly attributed to inhibiting lipid peroxidation, decreasing cholesterol and blood glucose levels, and lowering oxidative stress [55]. A recent study of the interaction between sex and sweetener can give us even more insight into the differential processing in the metabolism of flavanones and anthocyanins; indeed, the interaction of several compounds differs according to sex, which could lead to new studies related to hormone or physiological regulation [140]. *A. chilensis* leaf powders could be a potential substitute for synthetic antioxidants for the production of functional, clean-label beef patties with an extended shelf life, and the effect of leaf polyphenols on the growth of pathogenic and spoilage microorganisms in meat products means they are recommended [58]. Crisóstomo-Ayala et al [122] suggest that *A. chilensis* leaves could be an excellent source of antioxidants and lipophilic compounds for many industries, such as the nutraceutical and pharmaceutical industries.

4.6. *Ugni molinae* Turcz (Murtilla)

Ugni molinae Turcz (murtilla, murta or, uñi in mapudungun) is a native berry that is well-known for its antioxidant content [61]. This Chilean endemic wild bush is found in clear lands and forest margins in both the Coastal mountain range and in parts of the pre-Andean mountains, from Talca to the Palena river extending also towards the central valley [141]. However, it has also been reported in the island of Juan Fernández. *U. molinae* was first identified and classified in 1844 and was originally named *Myrtus ugni*. In spite of this, little scientific literature can be found to date, with respect to the identification and characterization of the compounds it contains. Native Chileans have transmitted and used the extracts from this species for health and cosmetic reasons for centuries. Alcoholic beverages and infusions have been made from their leaves mainly for reducing urinal tract pain, although aromatic, astringent, and stimulant properties have also been recorded for circulation dysfunctions [142]. As such, large numbers of balms and ointments from murta leaf extracts have appeared on the Chilean market during the last decade. The antioxidant and skin revitalizing properties of murta extracts have oxidative effects that prevent premature aging [12]. In this context, recent scientific studies report that this is partly due to the presence of multiple phenolic compounds with the ability to scavenge free radicals [62], [64]. The chemical composition of polyphenolic compounds such as flavonoids, coumarins, tannins and phenolic acids (gallic acid and catechin) has been determined in leaf extracts obtained with ethyl acetate and methanol, as well as saponins and sterols. Flavonols, myricetin, kaempferol and quercetin (as the main heterosides) were identified in a characterization study of *U. molinae* leaf extracts obtained at INIA-Carillanca Research Station, Chile (Figure 7). Epicatechin was present in alcoholic extracts and gallic acid derivatives were detected in water [13], [16].

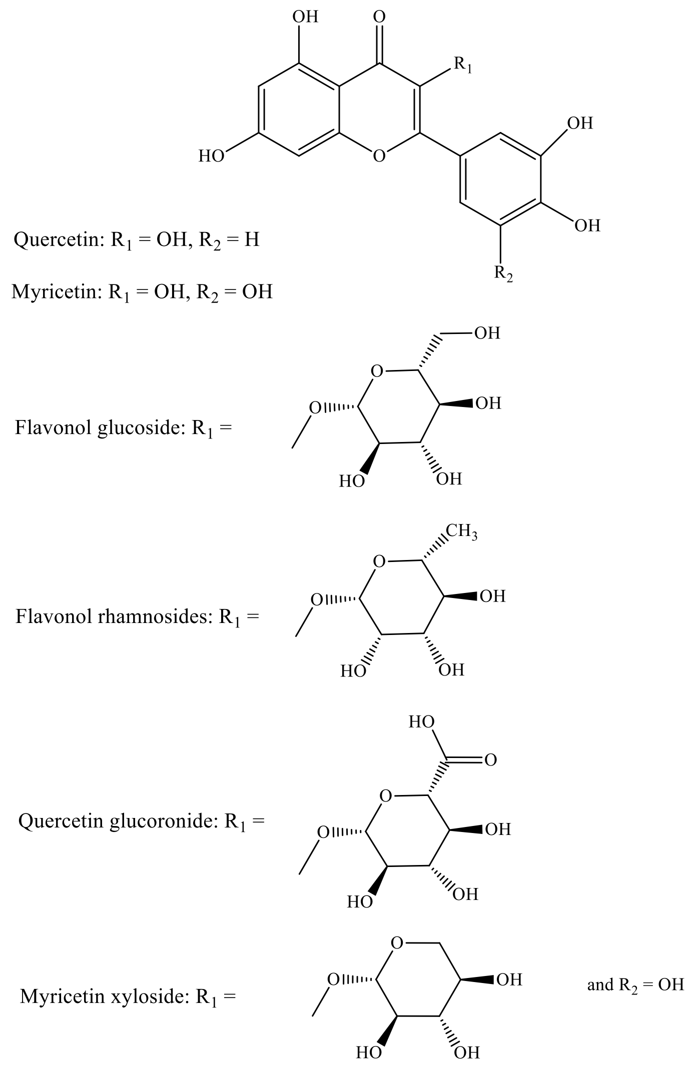

Figure 7. Chemical structure of flavonol glycosides detected in *U. molinae* Turcz leaves and fruits

An upward trend in polymerization was observed by the presence of polymeric complex compounds, which are interlinked in the form of sugars, proteins, etc. On the other hand, the differences in both phenolic composition and antioxidant efficiency in the alcoholic and aqueous extracts were lowered by the presence of these polymeric complex compounds. Antioxidant efficiency was assessed by two different methods. First, the capacity of the phenolic compounds to scavenge free radicals was expressed as a function of the percentage inhibition of either DPPH or EC50 (effective concentration 50). Second, due to differences in test results, the antioxidant power was also determined by TBARS. Results for the different extractions indicate the highest content of phenolic compounds in the methanol extract (44%) followed by the ethanol extract (40%) and finally by water (34%). Increasing temperature favored the extraction process, although not indefinitely, given the decreased stability of the phenolic compounds and the denaturation of membranes at temperatures above 50 ºC [16].

High DPPH inhibition percentage values were found in the methanol extract. Temperature is a factor that is inversely proportional to the inhibition percentage with longer extraction times. The lowest antioxidant efficiency values were obtained in the aqueous extract. EC50 showed an opposite trend compared to that of DPPH, due to the effectiveness of polar antioxidants in lipidic systems. Avello et al [143] explain this process on the basis of the protective effect exerted by the air-lipid interface created between the lipidic system and the hydrophilic extract against air-contact oxidation. By contrast, the authors observed that in the absence of this protection, the oxidation process was more active.

The analysis with HPLC-MS shows that the differences in the extracted phenolic compounds (by means of different solvents), are mainly due to both the phenolic composition and the degree of polymerization [16].

Pharmacological studies carried out on *U. molinae* leaf extracts confirm the antioxidant capacity of the fractions rich in polyphenolic compounds. Also, extracts produce antinociception in chemical and thermal pain models through a mechanism partially linked to either lipooxygenase and/or ciclooxygenase, via the arachidonic acid (AA) cascade and/or opioid receptors. Flavonoids, glycosides and triterpenoids have been isolated from the plant [12], [13], [144].

The antinociceptive activity of *U. molinae* extracts may be due to the presence of myricetin, quercetin and kaempferol glycosides. The anti-inflammatory activity is mainly caused by the presence of several pentacyclic triterpene acids, including the 2-α-hydroxyl derivatives alphitolic, asiatic, and corosolic acids (Figure 8). Betulinic, oleanolic and ursolic acids might be responsible for analgesic activities, as ursolic acid is a selective inhibitor of ciclooxygenase-2, and oleanolic acids may be involved in an opioid mechanism, and possibly, a modulatory influence on vanilloid receptors [68].

The preparation of *U. molinae* leaf extracts using solvents of increasing polarity facilitated the chemical bioguide study, allowing for the selective extraction of metabolites. Topical anti-inflammatory effects through the inhibition of enzymes involved in the synthesis of prostaglandins and leukotrienes, were also confirmed. This effect was attributed to a reduction in macrophage and complement activities, although it might also be due to the inhibition of the oxidative process. The pentacyclic triterpenes, betulinic, a mixture of olean and ursolic, alphitolic, corosolic, and asiatic acids, were isolated and identified from the extracts. The strong topical anti-inflammatory activities of *U. molinae* leaf extracts are consistent with the use of this plant material as a component in dermatological preparations. The anti-inflammatory activities are mainly caused by the presence of several pentacyclic triterpenes acids, including 2-α-hydroxyl derivatives alphitolic, asiatic and corosolic acids. The effects of alphitolic and asiatic acids on TPA-induced inflammation, and of corosolic acid on inflammation promoted by AA, have been reported [12]. Goity et al [145] isolated and identified asiatic, alphitolic, corosolic, betulinic, and a mixture of ursolic and oleanolic acids. The authors reported the presence of two triterpenoids not yet identified to date for this species: madecassic and maslinic acids. The results, showed that 2α-hydroxy pentacyclic triterpene acids (alphitolic, asiatic, corosolic, madecassic and maslinic acids), are more potent than indomethacin as anti-inflammatory agents, again reinforcing the fact that native plant species harbor vital potential in the pharmaceutical field due to their multiple, beneficial effects for human health [146].

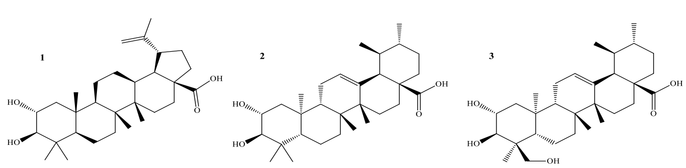

Figure 8. Alphitolic acid 1; corosolic acid 2 and asiatic acid 3.

The potential uses of *U. molinae* extract as an antimicrobial agent are supported by the presence of polyphenols, as a reduced number of these compounds have antimicrobial activity against a broad spectrum of microorganisms. Extracts from both fruits and leaves showed antimicrobial activity against *Staphylococcus aureus.* In addition, leaf extracts were efficient against *Klebsiella pneumoniae* and *Pseudomona aeruginosa*. Ethanol extracts exhibited either no antimicrobial activity or an activity that was significantly lower compared to an aqueous extract, thus presumably indicating that the water-soluble compounds (including polyphenols) have the highest antimicrobial activity. Leaf extracts were also more active against *S. aureus* than fruit extracts, likely attributable to the high proportion of phenols in the former. The antimicrobial activity of murtilla leaf and fruit extracts was significantly affected by the extraction solvent and/or the geographical location from where samples were obtained. Specifically, mountainous plant extracts were the most active against microbes, whilst fruit extracts were not as active as those from leaves, due to the lower level of antimicrobial compounds. Although the compounds responsible for the antimicrobial effect have not been identified, a study suggests that flavan-3-ols and flavonol glycosides might be the active agents [147].

Other studies have statistically confirmed that variations in polyphenol content in murtilla are partially due to the effect of the growing season, antioxidant activity and the dry matter content of murtilla fruits from three genotypes (the 14-4 genotype and the Red Pearl-INIA and South Pearl-INIA varieties). These characteristics tend to vary with atmospheric conditions such as rainfall and the number of frosts. In addition, polyphenol content and dry matter were affected by genotype [34]. Studies aimed at determining the phenolic composition and antioxidant capacity of *U. molinae* Turcz leaves across 10 different genotypes, showed significant differences between ellagitanins, gallic acid derivatives and flavonols, which influenced the composition and antioxidant activity of the genotypes analyzed [61]. On the other hand, due to the seasonality of the fruits, drying is an adequate technique for their preservation, thus proving an efficient method for maintaining the antioxidant properties of the polyphenolic components [66]. Several murtilla fruit drying studies have shown that the retention of polyphenolic compounds and antioxidant activity depend upon the temperature and technique of this process [125], [148], [149], [150], [151]. Alfaro et al [66] compared the effect of both conventional and freeze drying (FD) techniques on the retention of polyphenols as well as their antioxidant activity using identical genotypes (variety) of murtilla fruits. The application of FD on the Red Pearl-INIA variety of fresh *U. molinae* Turcz fruits preserved both the total polyphenol and the total anthocyanin contents with respect to fresh fruit. Hot-air drying at 65°C (HAD 65 ºC), hot-air drying at 80°C (HAD 80 ºC) and FD produced a variation in the composition of the polyphenols and anthocyanin compounds within the fresh fruits, thus showing that optimized post-harvest treatments are essential for preserving bioactive polyphenol compounds in murtilla berries. Vacuum drying might also prove to be an alternative drying method for preserving antioxidant activity and polyphenol composition in dried *U. molinae* Turcz [152]. The authors reported that quality parameters such as levels of phenolic compounds and antioxidant activity showed a slight decrease in value for the dried samples, although the results demonstrated that processed murta berries remain a key source of bioactive compounds. Another study showed that *U. molinae* Turcz fruit extracts are a natural source of antioxidants for protecting lipidic foods, such as soybean oil [153]. The high content of total dietary fiber (~50% by weight in fresh and processed berries) represents a novel functional property of these fruits [154].

4.7. *Berberis species*

B. microphylla (calafate). Calafate is a semi-evergreen shrub reaching heights of up to 3 m, distributed between the VI and XII Regions of Chile. Calafate fruits are a bluish-black berry containing malic acid, and are astringent in taste. The seeds occasionally have a toxic effect, due to the presence of berberine alkaloids [18], [155], which are most-abundant in roots. A total of 20 species belonging to the *Berberidaceae* family are described in Chile with *B. microphylla* G. Forst, being the most extensively distributed species. The fruits of all members are edible and possess high anthocyanin and hydroxycinnamic acid levels [18], [77]. In folk medicine, calafate is commonly used as either a laxative or infusion for fevers. Studies in Chile have shown that *B. microphylla* contains high anthocyanin and hydroxycinnamic acid derivative contents, with a substantial nutraceutical value for the prevention and control of chronic diseases and cardiovascular activity [77]. According to [18], [80], 16 flavonol derivatives and traces of isorhamnetin malonyl-hexoside, quercetin and kaempferol derivatives, and kaempferol aglycone were identified in methanolic extracts of *B. microphylla*. In recent years, calafate has also gained importance due to its interesting pharmacological [156], [157], [158], antifungal [159], [160], [161], antioxidant [77], [162], and antibacterial properties [160], based on the presence of both alkaloids and polyphenolic compounds. The alkaloid extracts from *B. microphylla* leaves, stems and roots have selective antibacterial activity against Gram-positive bacterial strains [163]. A total of eleven alkaloids were identified in this specie using HPLC ESI-MS/MS; isocorydine, jatrorrhizine, palmatine, reticuline, scoulerine, tetrahydroberberine and thalifendine, allocryptopine, berberine, calafatine and protopine. Additionally, the presence of these alkaloids was organ-specific and may be affected by environmental conditions [78]. Indeed, *B. microphylla* leaves show high phenotypic plasticity between different culture sites. Changes in leaf morphology and structure are an indication that the plants are adjusting to the new culture conditions i.e., higher temperatures and lower irradiance [79], [164]. High concentrations of anthocyanins and hydroxycinnamic acid derivatives [17.81 μmol/g and 2.62 μmol/g fresh weight (FW), respectively] are present in this fruit [80]. The total flavonol concentration is 1.33 μmol/g, of which glycosyl metabolites of quercetin and isorhamnetin were the most abundant. The phenolic acid compounds identified in *B. microphylla* included gallic, chlorogenic, caffeic, coumaric and ferulic acids, as well as flavonoids such as rutin, myricetin, quercetin and kaempferol. Similar profiles were observed in calafate from distinct locations [79]. Differences in quantitative and qualitative compositions of phenolic compounds and antioxidant activities of *B. micropylla* were also related to agronomic management practices, growing season and climatic conditions [76]. Calafate pulp and skin have higher flavonol concentrations than seeds, levels that fall during ripening, whilst berberine was the only compound detected in the fruit (0.001%), mainly in seeds [77].

B. darwinii (Michay). Michay is a shrub that grows in the pre-Andean mountains in Chile from the VII to the XI Region, and in Argentina to the west of Rio Negro and Neuquén [165]. It reaches heights of up to 1.5 m, and its fruits are bluish-black with seeds rich in amygdalin, a compound that deters herbivore feeding. Few studies on the properties of the fruits have been reported, although it is known that plant extracts inhibit immune responses *in vitro* [156]. Several alkaloids have been reported to be present in the plant [19], and berberine may be found in the fruits. With respect to the presence of polyphenol compounds in *B. darwinii*, the absence of isorhamnetin-3-rutinoside and isorhamnetin-3-galactoside was reported, although this berry showed a similar flavonols content as *B. microphylla* and other *Berberis* members [18], [77], [155].

CONCLUSIONS

The presence of high concentrations of bioactive compounds such as polyphenols, anthocyanins, and other key compounds such as alkaloids and terpenes in native species from southern Chile, has been linked to beneficial effects on human health. Polyphenol compounds play a crucial role in the incidence and morbidity rate of chronical diseases such as diabetes, hypertension, cancer, aging and obesity. These compounds contribute towards preventing the appearance and recurrence of such illnesses by disrupting chain oxidation reactions in cellular components and by increasing plasma antioxidant activity. Extracts of berries such as maqui, murtilla and calafate have high antioxidant activities and have therefore been classified as superfruits. Other native plants, like boldo, matico and bailahuen are recognized as medicinal plants by their hepatoprotective, healing and antioxidant effects. However, several modes of action and the protective effects of polyphenols are yet unclear. Hence, expanding the scientific knowledge of variables such as absorption, distribution and elimination of polyphenols will increase our understanding of their benefits to human health. In this sense, it is recommended the factors that affect the bioavailability of polyphenols be considered to be used in the industry.

ABBREVIATIONS

TRAP, total radical-trapping potential; TAR, total antioxidant reactivity; LDL, low-density lipoproteins; DNA, Desoxyribonucleic Acid; AAPH, 2,2'-Azo-bis(2-amidinopropano) dihydrochloro; DPPH, 2,2-difenyl-1-picrylhydrazyl; ORAC, Oxygen Radical Absorbance Capacity; AOA, antioxidant capacity; *f* stoichiometric coefficient of initiation; $R_,$ Oxidation inhibition ratio; R_{IN}, Initiation ratio; TBARS, thiobarbituric acid reactive substances; ABTS, 2,2′–azino-bis (3-ethylbenztiazolino 6-sulfonic acid); TPA (12-0-tetradecanoylphorbol-13-acetate); AA, Arachidonic Acid

REFERENCE

1] M. Montes, T. Wilkomirsky, and L. Valenzuela, *Plantas Medicinales*. Concepción: Ediciones Universidad de Concepción, 1992.

[2] H. Vogel *et al.*, "Antioxidant properties and TLC characterization of four Chilean Haplopappus-species known as bailahuén.," *J Ethnopharmacol*, vol. 97, no. 1, pp. 97–100, Feb. 2005, doi: 10.1016/j.jep.2004.10.027.

[3] H. Speisky and B. K. Cassels, "Boldo and boldine: an emerging case of natural drug development," *Pharmacol Res*, vol. 29, no. 1, pp. 1–12, Jan. 1994, doi: 10.1016/1043-6618(94)80093-6.

[4] L. Velázquez, J. Quiñones, R. Díaz, M. Pateiro, J. M. Lorenzo, and N. Sepúlveda, "Natural antioxidants from endemic leaves in the elaboration of processed meat products: Current status," *Antioxidants*, vol. 10, no. 9, pp. 1–18, 2021, doi: 10.3390/antiox10091396.

[5] S. Kohli *et al.*, "In-vitro evaluation of the effectiveness of polyphenols based strawberry extracts for dental bleaching," *Sci Rep*, vol. 13, no. 1, p. 4181, Mar. 2023, doi: 10.1038/s41598-023-31125-6.

[6] M. J. Simirgiotis and G. Schmeda-Hirschmann, "Direct identification of phenolic constituents in Boldo Folium (Peumus boldus Mol.) infusions by high-performance liquid chromatography with diode array detection and electrospray ionization tandem mass spectrometry," *J Chromatogr A*, vol. 1217, no. 4, pp. 443–449, Jan. 2010, doi: 10.1016/j.chroma.2009.11.014.

[7] G. Schmeda-Hirschmann, J. A. Rodriguez, C. Theoduloz, S. L. Astudillo, G. E. Feresin, and A. Tapia, "Free-radical Scavengers and Antioxidants from Peumus boldus Mol. ('Boldo')," *Free Radic Res*, vol. 37, no. 4, pp. 447–452, Jan. 2003, doi: 10.1080/1071576031000090000.

[8] P. O'Brien, C. Carrasco-Pozo, and H. Speisky, "Boldine and its antioxidant or health-promoting properties," *Chem Biol Interact*, vol. 159, no. 1, pp. 1–17, Jan. 2006, doi: 10.1016/j.cbi.2005.09.002.

[9] E. Alarcón, A. M. Campos, A. Edwards, E. Lissi, and C. López-Alarcón, "Antioxidant capacity of herbal infusions and tea extracts: A comparison of ORAC-fluorescein and ORAC-pyrogallol red methodologies," *Food Chem*, vol. 107, no. 3, pp. 1114–1119, Apr. 2008, doi: 10.1016/j.foodchem.2007.09.035.

[10] N. Backhouse *et al.*, "Analgesic, anti-inflammatory and antioxidant properties of *Buddleja globosa*, Buddlejaceae," *J Ethnopharmacol*, vol. 116, no. 2, pp. 263–269, Mar. 2008, doi: 10.1016/j.jep.2007.11.025.

[11] I. M. Villaseñor, A. P. Canlas, K. M. Faustino, and K. G. Plana, "Evaluation of the bioactivity of triterpene mixture isolated from *Carmona retusa* (Vahl.) Masam leaves," *J Ethnopharmacol*, vol. 92, no. 1, pp. 53–56, May 2004, doi: 10.1016/j.jep.2004.01.017.

[12] M. C. Aguirre *et al.*, "Topical anti-inflammatory activity of 2α-hydroxy pentacyclic triterpene acids from the leaves of *Ugni molinae*," *Bioorg Med Chem*, vol. 14, no. 16, pp. 5673–5677, 2006, doi: 10.1016/j.bmc.2006.04.021.

[13] M. Avello and E. Pastene, "Actividad Antioxidante de infusos de *Ugni Molinae* Turcz ('Murtilla').," *Bol Latinoam Caribe Plantas Med Aromat*, vol. 4, no. 002, pp. 33–39, 2005.

[14] F. Ávila, C. Theoduloz, C. López-Alarcón, E. Dorta, and G. Schmeda-Hirschmann, "Cytoprotective Mechanisms Mediated by Polyphenols from Chilean Native Berries against Free Radical-Induced Damage on AGS Cells," *Oxid Med Cell Longev*, vol. 2017, pp. 1–13, 2017, doi: 10.1155/2017/9808520.

[15] S. Miranda-Rottmann, A. A. Aspillaga, D. D. Pérez, L. Vasquez, A. L. F. Martinez, and F. Leighton, "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*, vol. 50, no. 26, pp. 7542–7547, Dec. 2002, doi: 10.1021/jf025797n.

[16] M. Rubilar, M. Pinelo, M. Ihl, E. Scheuermann, J. Sineiro, and M. J. Nuñez, "Murta Leaves (*Ugni molinae* Turcz) as a Source of Antioxidant Polyphenols," *J Agric Food Chem*, vol. 54, no. 1, pp. 59–64, Jan. 2006, doi: 10.1021/jf051571j.

[17] J. Cheel, C. Theoduloz, J. A. Rodríguez, P. D. S. Caligari, and G. Schmeda-Hirschmann, “Free radical scavenging activity and phenolic content in achenes and thalamus from *Fragaria chiloensis* ssp. chiloensis, F. vesca and F. x ananassa cv. Chandler,” *Food Chem*, vol. 102, no. 1, pp. 36–44, 2007, doi: 10.1016/j.foodchem.2006.04.036.

[18] A. Ruiz *et al.*, “Isolation and Structural Elucidation of Anthocyanidin 3,7-β- O -Diglucosides and Caffeoyl-glucaric Acids from Calafate Berries,” *J Agric Food Chem*, vol. 62, no. 29, pp. 6918–6925, Jul. 2014, doi: 10.1021/jf5012825.

[19] J. Echeverría and H. Niemeyer, “Alkaloids from the native flora of Chile: a review,” *Bol Latinoam Caribe Plantas Med Aromat*, vol. 11, no. 4, pp. 291–305, 2012.

[20] J. B. Harborne, “Plants Phenolics,” in *Secondary Plant Products*, 1st ed., E. A. Bell and B. V. Charlwood, Eds., Springer-Verlag Berlin Heidelberg, 1980, pp. 329–395.

[21] Y. Lin, J. Fang, Z. Zhang, M. A. Farag, Z. Li, and P. Shao, “Plant flavonoids bioavailability in vivo and mechanisms of benefits on chronic kidney disease: a comprehensive review,” *Phytochemistry Reviews*, vol. 0123456789, Sep. 2022, doi: 10.1007/s11101-022-09837-w.

[22] M. Gallon, M. Cortés, J. Gil Gonzalez, A. Lahlou, and J. L. Guil-Guerrero, “Influence of Storage Variables on the Antioxidant and Antitumor Activities, Phenolic Compounds and Vitamin C of an Agglomerate of Andean Berries,” *SSRN Electronic Journal*, vol. 9, no. September 2022, 2022, doi: 10.2139/ssrn.4220980.

[23] I. Urquiaga and F. Leighton, “Plant Polyphenol Antioxidants and Oxidative Stress,” *Biol Res*, vol. 33, no. 2, pp. 55–64, 2000, doi: 10.4067/S0716-97602000000200004.

[24] A. Crozier *et al.*, “Antioxidant flavonols from fruits, vegetables and beverages: measurements and bioavailability,” *Biol Res*, vol. 33, no. 2, pp. 79–88, 2000, doi: 10.4067/S0716-97602000000200007.

[25] J.-M. Rouanet *et al.*, “Berry juices, teas, antioxidants and the prevention of atherosclerosis in hamsters,” *Food Chem*, vol. 118, no. 2, pp. 266–271, Jan. 2010, doi: 10.1016/j.foodchem.2009.04.116.

[26] H. Kamei *et al.*, “Suppression of Tumor Cell Growth by Anthocyanins In Vitro,” *Cancer Invest*, vol. 13, no. 6, pp. 590–594, Jan. 1995, doi: 10.3109/07357909509024927.

[27] N. P. Seeram, Y. Zhang, and M. G. Nair, “Inhibition of Proliferation of Human Cancer Cells and Cyclooxygenase Enzymes by Anthocyanidins and Catechins,” *Nutr Cancer*, vol. 46, no. 1, pp. 101–106, May 2003, doi: 10.1207/S15327914NC4601_13.

[28] L. Y. Foo, Y. Lu, A. B. Howell, and N. Vorsa, “The structure of cranberry proanthocyanidins which inhibit adherence of uropathogenic P-fimbriated Escherichia coli in vitro,” *Phytochemistry*, vol. 54, no. 2, pp. 173–181, May 2000, doi: 10.1016/S0031-9422(99)00573-7.

[29] A. B. Howell, “Bioactive compounds in cranberries and their role in prevention of urinary tract infections,” *Mol Nutr Food Res*, vol. 51, no. 6, pp. 732–737, Jun. 2007, doi: 10.1002/mnfr.200700038.

[30] A. B. Howell, J. D. Reed, C. G. Krueger, R. Winterbottom, D. G. Cunningham, and M. Leahy, “A-type cranberry proanthocyanidins and uropathogenic bacterial anti-adhesion activity,” *Phytochemistry*, vol. 66, no. 18, pp. 2281–2291, Sep. 2005, doi: 10.1016/j.phytochem.2005.05.022.

[31] T. F. Barberán, “Los polifenoles de los alimentos y la salud,” *Alimentación, nutrición y salud*, vol. 10, no. 2, pp. 41–53, 2003.

[32] B. W. Bolling, J. B. Blumberg, and C.-Y. Oliver Chen, “The influence of roasting, pasteurisation, and storage on the polyphenol content and antioxidant capacity of California almond skins,” *Food Chem*, vol. 123, no. 4, pp. 1040–1047, Dec. 2010, doi: 10.1016/j.foodchem.2010.05.058.

[33] A. A. van der Sluis, M. Dekker, A. de Jager, and W. M. F. Jongen, “Activity and Concentration of Polyphenolic Antioxidants in Apple: Effect of Cultivar, Harvest Year, and Storage Conditions,” *J Agric Food Chem*, vol. 49, no. 8, pp. 3606–3613, Aug. 2001, doi: 10.1021/jf001493u.

[34] S. Alfaro, A. Mutis, and R. Palma, “Influence of genotype and harvest year on polyphenol content and antioxidant activity in murtilla (Ugni molinae Turcz) fruit,” *J Soil Sci Plant Nutr*, vol. 13, no. 1, pp. 67–78, 2013.

[35] L. Astudillo, J. a Rodriguez, and G. Schmeda-Hirschmann, “Gastroprotective activity of oleanolic acid derivatives on experimentally induced gastric lesions in rats and mice,” *Journal of Pharmacy and Pharmacology*, vol. 54, no. 4, pp. 583–588, Apr. 2002, doi: 10.1211/0022357021778718.

[36] S. Molares and A. Ladio, “Ethnobotanical review of the Mapuche medicinal flora: Use patterns on a regional scale,” *J Ethnopharmacol*, vol. 122, no. 2, pp. 251–260, Mar. 2009, doi: 10.1016/j.jep.2009.01.003.

[37] M. Heinrich, A. Ankli, B. Frei, C. Weimann, and O. Sticher, “Medicinal plants in Mexico: healers’ consensus and cultural importance,” *Soc Sci Med*, vol. 47, no. 11, pp. 1859–1871, Dec. 1998, doi: 10.1016/S0277-9536(98)00181-6.

[38] A. Gironés-Vilaplana, N. Baenas, D. Villaño, H. Speisky, C. García-Viguera, and D. A. Moreno, “Evaluation of Latin-American fruits rich in phytochemicals with biological effects,” *J Funct Foods*, vol. 7, pp. 599–608, Mar. 2014, doi: 10.1016/j.jff.2013.12.025.

[39] M. Rubilar *et al.*, “Extracts of Maqui (Aristotelia chilensis) and Murta (Ugni molinae Turcz.): Sources of Antioxidant Compounds and α-Glucosidase/α-Amylase Inhibitors,” *J Agric Food Chem*, vol. 59, no. 5, pp. 1630–1637, Mar. 2011, doi: 10.1021/jf103461k.

[40] J. Cheel, C. Theoduloz, J. a. Rodríguez, P. D. S. Caligari, and G. Schmeda-Hirschmann, “Free radical scavenging activity and phenolic content in achenes and thalamus from Fragaria chiloensis ssp. chiloensis, F. vesca and F. x ananassa cv. Chandler,” *Food Chem*, vol. 102, no. 1, pp. 36–44, Jan. 2007, doi: 10.1016/j.foodchem.2006.04.036.

[41] M. J. Simirgiotis, C. Theoduloz, P. D. S. Caligari, and G. Schmeda-Hirschmann, “Comparison of phenolic composition and antioxidant properties of two native Chilean and one domestic strawberry genotypes,” *Food Chem*, vol. 113, no. 2, pp. 377–385, Mar. 2009, doi: 10.1016/j.foodchem.2008.07.043.

[42] R. Torres, C. Mascayano, C. N????ez, B. Modak, and F. Faini, “Coumarins of haplopappus multifolius and derivative as inhibitors of lox: Evaluation in-vitro and docking studies,” *Journal of the Chilean Chemical Society*, vol. 58, no. 4, pp. 2027–2030, 2013.

[43] R. Torres, F. Faini, F. D. Monache, and G. D. Monache, “Two new O-geranyl coumarins from the resinous exudate of Haplopappus multifolius,” *Fitoterapia*, vol. 75, no. 1, pp. 5–8, Jan. 2004, doi: 10.1016/j.fitote.2003.06.003.

[44] F. Faini, C. Labbé, R. Torres, J. M. Rodilla, L. Silva, and F. D. Monache, “New phenolic esters from the resinous exudate of Haplopappus taeda,” *Fitoterapia*, vol. 78, no. 7–8, pp. 611–613, 2007, doi: 10.1016/j.fitote.2007.06.006.

[45] F. Faini, R. Torres, J. M. Rodilla, C. Labbé, C. Delporte, and F. Jaña, “Chemistry and bioactivity of Haplopappus remyanus (‘bailahuen’), a chilean medicinal plant,” *J Braz Chem Soc*, vol. 22, no. 12, pp. 2344–2349, Dec. 2011, doi: 10.1590/S0103-50532011001200015.

[46] Y. S. Lau, X. Y. Tian, Y. Huang, D. Murugan, F. I. Achike, and M. R. Mustafa, “Boldine protects endothelial function in hyperglycemia-induced oxidative stress through an antioxidant mechanism,” *Biochem Pharmacol*, vol. 85, no. 3, pp. 367–375, Feb. 2013, doi: 10.1016/j.bcp.2012.11.010.

[47] N. H. Turgut, H. Gungor, M. Ekici, M. A. Erdogan, M. O. Karayigit, and H. Kara, “Boldine provides protective effect against nephrotoxicity induced by cisplatin in Wistar rats: Role of oxidative stress, inflammation and caspase-3,” *Biocell*, vol. 46, no. 6, pp. 2111–2122, 2022, doi: 10.32604/biocell.2022.020383.

[48] N. Quezada, M. Asencio, J. M. Valle, J. M. Aguilera, and B. Gómez, "Antioxidant Activity of Crude Extract, Alkaloid Fraction, and Flavonoid Fraction from Boldo (Peumus boldus Molina) Leaves," *J Food Sci*, vol. 69, no. 5, pp. C371–C376, May 2006, doi: 10.1111/j.1365-2621.2004.tb10700.x.

[49] C. V. Klimaczewski *et al.*, "Antioxidant activity of Peumus boldus extract and alkaloid boldine against damage induced by Fe(II)–citrate in rat liver mitochondria in vitro," *Ind Crops Prod*, vol. 54, pp. 240–247, Mar. 2014, doi: 10.1016/j.indcrop.2013.11.051.

[50] C. Soto, E. Caballero, E. Pérez, and M. E. Zúñiga, "Effect of extraction conditions on total phenolic content and antioxidant capacity of pretreated wild Peumus boldus leaves from Chile," *Food and Bioproducts Processing*, vol. 92, no. 3, pp. 328–333, Jul. 2014, doi: 10.1016/j.fbp.2013.06.002.

[51] J. Fernández, P. Lagos, P. Rivera, and E. Zamorano-Ponce, "Effect of boldo (Peumus boldus Molina) infusion on lipoperoxidation induced by cisplatin in mice liver," *Phytotherapy Research*, vol. 23, no. 7, pp. 1024–1027, Jul. 2009, doi: 10.1002/ptr.2746.

[52] C. Otero *et al.*, "Biochemical characterization of Peumus boldus fruits: Insights of its antioxidant properties through a theoretical approach," *Food Chem*, vol. 370, no. September 2021, p. 131012, Feb. 2022, doi: 10.1016/j.foodchem.2021.131012.

[53] P. Velásquez, M. I. Sandoval, A. Giordano, M. Gómez, and G. Montenegro, "Nutritional Composition and Polyphenolic Content of Edible Peumus boldus Mol. Fruits.," *Cienc Investig Agrar*, vol. 44, no. 1, pp. 1–11, Apr. 2017, doi: 10.7764/rcia.v44i1.1684.

[54] B. González, H. Vogel, I. Razmilic, and E. Wolfram, "Polyphenol, anthocyanin and antioxidant content in different parts of maqui fruits (*Aristotelia chilensis*) during ripening and conservation treatments after harvest.," *Ind Crops Prod*, vol. 76, pp. 158–165, 2015, doi: 10.1016/j.indcrop.2015.06.038.

[55] L. Rodríguez *et al.*, "A Comprehensive Literature Review on Cardioprotective Effects of Bioactive Compounds Present in Fruits of Aristotelia chilensis Stuntz (Maqui)," *Molecules*, vol. 27, no. 19, 2022, doi: 10.3390/molecules27196147.

[56] M. T. Escribano-Bailón, C. Alcalde-Eon, O. Muñoz, J. C. Rivas-Gonzalo, and C. Santos-Buelga, "Anthocyanins in berries of Maqui [Aristotelia chilensis (Mol.) Stuntz]," *Phytochemical Analysis*, vol. 17, no. 1, pp. 8–14, Jan. 2006, doi: 10.1002/pca.872.

[57] B. Salehi *et al.*, "Ethnopharmacology, Phytochemistry and Biological Activities of Native Chilean Plants," *Curr Pharm Des*, vol. 27, no. 7, pp. 953–970, 2020, doi: 10.2174/1381612826666201124105623.

[58] L. Velázquez *et al.*, "Maqui (Aristotelia chilensis (Mol.) Stuntz): A Natural Antioxidant to Improve Quality of Meat Patties," *Antioxidants*, vol. 11, no. 7, 2022, doi: 10.3390/antiox11071405.

[59] V. Romanucci *et al.*, "Bioactive Compounds of Aristotelia chilensis Stuntz and their Pharmacological Effects," *Curr Pharm Biotechnol*, vol. 17, no. 6, pp. 513–523, Apr. 2016, doi: 10.2174/1389201017666160114095246.

[60] A. Gironés-Vilaplana, P. Mena, C. García-Viguera, and D. A. Moreno, "A novel beverage rich in antioxidant phenolics: Maqui berry (Aristotelia chilensis) and lemon juice," *LWT - Food Science and Technology*, vol. 47, no. 2, pp. 279–286, Jul. 2012, doi: 10.1016/j.lwt.2012.01.020.

[61] M. Peña-Cerda *et al.*, "Phenolic composition and antioxidant capacity of Ugni molinae Turcz. leaves of different genotypes," *Food Chem*, vol. 215, no. 15, pp. 219–227, Jan. 2017, doi: 10.1016/j.foodchem.2016.07.159.

[62] J. López, A. Vega-Gálvez, A. Rodríguez, E. Uribe, and C. Bilbao-Sainz, "Murta (Ugni molinae Turcz.): A review on chemical composition, functional components and biological activities of leaves and fruits," *Chilean Journal of Agricultural and Animal Sciences*, vol. 34, no. 1, 2018, doi: 10.4067/s0719-38902018005000205.

[63] V. Bifani, C. Ramírez, M. Ihl, M. Rubilar, A. García, and N. Zaritzky, "Effects of murta (Ugni molinae Turcz) extract on gas and water vapor permeability of carboxymethylcellulose-based edible films," *LWT - Food Science and Technology*, vol. 40, no. 8, pp. 1473–1481, Oct. 2007, doi: 10.1016/j.lwt.2006.03.011.

[64] R. I. Castro, P. Ramos, C. Parra-Palma, and L. Morales-Quintana, "Ugni molinae Fruit as a Source of Bioactive Compounds with Good Quality Traits," *Biomed Res Int*, vol. 2021, 2021, doi: 10.1155/2021/6683877.

[65] M. Junqueira-Gonçalves, L. Yáñez, C. Morales, M. Navarro, R. A. Contreras, and G. Zúñiga, "Isolation and Characterization of Phenolic Compounds and Anthocyanins from Murta (Ugni molinae Turcz.) Fruits. Assessment of Antioxidant and Antibacterial Activity," *Molecules*, vol. 20, no. 4, pp. 5698–5713, Mar. 2015, doi: 10.3390/molecules20045698.

[66] S. Alfaro, A. Mutis, A. Quiroz, I. Seguel, and E. Scheuermann, "Effects of Drying Techniques on Murtilla Fruit Polyphenols and Antioxidant Activity," *J Food Res*, vol. 3, no. 5, pp. 73–82, 2014, doi: 10.5539/jfr.v3n5p73.

[67] E. Scheuermann *et al.*, "Effects of Packaging and Preservation Treatments on the Shelf Life of Murtilla Fruit (Ugni molinae Turcz) in Cold Storage," *Packaging Technology and Science*, vol. 27, no. 3, pp. 241–248, Mar. 2014, doi: 10.1002/pts.2014.

[68] C. Delporte *et al.*, "Analgesic activity of Ugni molinae (murtilla) in mice models of acute pain," *J Ethnopharmacol*, vol. 112, no. 1, pp. 162–165, 2007, doi: 10.1016/j.jep.2007.02.018.

[69] M. Suwalsky, P. Orellana, M. Avello, F. Villena, and C. P. Sotomayor, "Human erythrocytes are affected in vitro by extracts of Ugni molinae leaves," *Food and Chemical Toxicology*, vol. 44, no. 8, pp. 1393–1398, Aug. 2006, doi: 10.1016/j.fct.2006.03.003.

[70] J. Torres-Vega, S. Gómez-Alonso, J. Pérez-Navarro, J. Alarcón-Enos, and E. Pastene-Navarrete, "Polyphenolic compounds extracted and purified from buddleja globosa hope (Buddlejaceae) leaves using natural deep eutectic solvents and centrifugal partition chromatography," *Molecules*, vol. 26, no. 8, 2021, doi: 10.3390/molecules26082192.

[71] P. Zamorano-Aguilar, M. Morales, Y. Rivillas, J. López, and B. A. Rojano, "Antioxidant activity and cytotoxic effect of Chilean Buddleja globosa (matico) and Ribes magellanicum (zarzaparrilla) flower extracts," *Acta Scientiarum Polonorum, Hortorum Cultus*, vol. 19, no. 6, pp. 59–70, 2020, doi: 10.24326/ASPHC.2020.6.5.

[72] M. Fuentes, C. Sepúlveda, M. Alarcón, I. Palomo, and E. Fuentes, "Buddleja globosa (matico) prevents collagen-induced platelet activation by decreasing phospholipase C-gamma 2 and protein kinase C phosphorylation signaling," *J Tradit Complement Med*, vol. 8, no. 1, pp. 66–71, 2018, doi: 10.1016/j.jtcme.2017.02.005.

[73] N. Backhouse *et al.*, "Antinociceptive activity of Buddleja globosa (matico) in several models of pain," *J Ethnopharmacol*, vol. 119, no. 1, pp. 160–165, Sep. 2008, doi: 10.1016/j.jep.2008.06.022.

[74] N. Backhouse *et al.*, "Analgesic, anti-inflammatory and antioxidant properties of Buddleja globosa, Buddlejaceae," *J Ethnopharmacol*, vol. 116, no. 2, pp. 263–269, Mar. 2008, doi: 10.1016/j.jep.2007.11.025.

[75] M. F. Chamorro *et al.*, "Polyphenol Composition and (Bio)Activity of Berberis Species and Wild Strawberry from the Argentinean Patagonia," *Molecules*, vol. 24, no. 18, p. 3331, Sep. 2019, doi: 10.3390/molecules24183331.

[76] M. E. Arena, P. D. Postemsky, and N. R. Curvetto, "Changes in the phenolic compounds and antioxidant capacity of Berberis microphylla G. Forst. berries in relation to light intensity and fertilization," *Sci Hortic*, vol. 218, pp. 63–71, 2017, doi: 10.1016/j.scienta.2017.02.004.

[77] A. Ruiz *et al.*, "Flavonols, Alkaloids, and Antioxidant Capacity of Edible Wild Berberis Species from Patagonia," *J Agric Food Chem*, vol. 62, no. 51, pp. 12407–12417, Dec. 2014, doi: 10.1021/jf502929z.

[78] L. Manosalva, A. Mutis, J. Díaz, A. Urzúa, V. Fajardo, and A. Quiroz, "Identification of isoquinoline alkaloids from berberis microphylla by HPLC ESI-MS/MS," *Bol Latinoam Caribe Plantas Med Aromat*, vol. 13, no. 4, pp. 324–335, 2014.

[79] E. Mariangel, M. Reyes-Diaz, W. Lobos, E. Bensch, H. Schalchli, and P. Ibarra, "The antioxidant properties of calafate (Berberis microphylla) fruits from four different locations in southern Chile," *Cienc Investig Agrar*, vol. 40, no. 1, pp. 161–170, Apr. 2013, doi: 10.4067/S0718-16202013000100014.

[80] A. Ruiz *et al.*, "Polyphenols and Antioxidant Activity of Calafate (Berberis microphylla) Fruits and Other Native Berries from Southern Chile," *J Agric Food Chem*, vol. 58, no. 10, pp. 6081–6089, May 2010, doi: 10.1021/jf100173x.

[81] A. Hoffmann, *Flora silvestre de Chile : zona araucana : una guía ilustrada para la identificación de las especies de plantas leñosas del sur de Chile (entre el río Maule y el seno de Reloncaví)*, 4ª., vol. 1. Santiago, 1997.

[82] A. Srivastava, P. Tandon, A. P. Ayala, and S. Jain, "Solid state characterization of an antioxidant alkaloid boldine using vibrational spectroscopy and quantum chemical calculations," *Vib Spectrosc*, vol. 56, no. 1, pp. 82–88, May 2011, doi: 10.1016/j.vibspec.2010.08.001.

[83] T. Boeing *et al.*, "Gastroprotective effect of the alkaloid boldine: Involvement of non-protein sulfhydryl groups, prostanoids and reduction on oxidative stress," *Chem Biol Interact*, vol. 327, no. March, p. 109166, Aug. 2020, doi: 10.1016/j.cbi.2020.109166.

[84] A. A. Refaie *et al.*, "Hepatoprotective Impact of Boldo (Peumus Boldus) Extract against Azoxystrobin Induced DNA Damage, Gene Expression Modulation, Biochemical and Histopathological Alterations Mediated-ROS Generation in Male Rats," *Egypt J Chem*, vol. 65, no. 8, pp. 687–698, 2022, doi: 10.21608/ejchem.2022.120306.5401.

[85] C. Ferrante *et al.*, "Phenolic Content and Antimicrobial and," *Antibiotics*, vol. 9, p. 783, 2020.

[86] A. Valenzuela, S. Nieto, B. K. Cassels, and H. Speisky, "Inhibitory effect of boldine on fish oil oxidation," *J Am Oil Chem Soc*, vol. 68, no. 12, pp. 935–937, Dec. 1991, doi: 10.1007/BF02657538.

[87] J. M. Del Valle, C. Godoy, M. Asencio, and J. M. Aguilera, "Recovery of antioxidants from boldo (Peumus boldus M.) by conventional and supercritical CO2 extraction," *Food Research International*, vol. 37, pp. 695–702, 2004, doi: 10.1016/j.foodres.2003.03.001.

[88] L. Lara-Fernández, H. De Garza-Toledo, J. E. Wong-Paz, R. Belmares, R. Rodríguez-Herrera, and C. N. Aguilar, "Separation conditions and evaluation of antioxidant properties of boldo (Peumus boldus) extracts," *J Med Plant Res*, vol. 7, no. 15, pp. 911–917, 2013, doi: 10.5897/JMPR13.2562.

[89] W. Naser, "The cosmetic effects of various natural biofunctional ingredients against skin aging: A review," *International Journal of Applied Pharmaceutics*, vol. 13, no. 1, pp. 10–18, 2021, doi: 10.22159/ijap.2021v13i1.39806.

[90] G. Silva-Aguayo *et al.*, "Essential oil of Peumus boldus Molina against the nematode Haemonchus contortus (L3) and three stored cereal insect pests," *Chil J Agric Res*, vol. 81, no. 3, pp. 390–397, 2021, doi: 10.4067/S0718-58392021000300390.

[91] G. Schmeda-Hirschmann, C. Quispe, and B. González, "Phenolic Profiling of the South American 'Baylahuen' Tea (Haplopappus spp., Asteraceae) by HPLC-DAD-ESI-MS," *Molecules*, vol. 20, no. 1, pp. 913–928, Jan. 2015, doi: 10.3390/molecules20010913.

[92] G. Schmeda-Hirschmann, C. Quispe, and B. González, "Phenolic Profiling of the South American 'Baylahuen' Tea (Haplopappus spp., Asteraceae) by HPLC-DAD-ESI-MS," *Molecules*, vol. 20, no. 1, pp. 913–928, Jan. 2015, doi: 10.3390/molecules20010913.

[93] C. Zdero, F. Bohlmann, and H. M. Niemeyer, "Friedolabdanes and other constituents from chilean Haplopappus species," *Phytochemistry*, vol. 30, no. 11, pp. 3669–3677, 1991, doi: 10.1016/0031-9422(91)80089-J.

[94] N. Ünal and V. Okatan, "Effects of drought stress treatment on phytochemical contents of strawberry varieties," *Sci Hortic*, vol. 316, no. February, p. 112013, 2023, doi: 10.1016/j.scienta.2023.112013.

[95] N. Araya *et al.*, "Formulation of water-soluble Buddleja globosa Hope extracts and characterization of their antimicrobial properties against Pseudomonas aeruginosa," *Front Pharmacol*, vol. 13, no. November, pp. 1–11, Nov. 2022, doi: 10.3389/fphar.2022.921511.

[96] S. Khan, H. Ullah, and L. Zhang, "Bioactive constituents form Buddleja species," *Pak J Pharm Sci*, vol. 32, no. 2, pp. 721–741, 2019.

[97] L. Letelier, C. Gaete-Eastman, P. Peñailillo, M. A. Moya-León, and R. Herrera, "Southern Species From the Biodiversity Hotspot of Central Chile: A Source of Color, Aroma, and Metabolites for Global Agriculture and Food Industry in a Scenario of Climate Change," *Front Plant Sci*, vol. 11, no. July, pp. 1–16, 2020, doi: 10.3389/fpls.2020.01002.

[98] P. J. Houghton, P. J. Hylands, A. Y. Mensah, A. Hensel, and A. M. Deters, "In vitro tests and ethnopharmacological investigations: Wound healing as an example," *J Ethnopharmacol*, vol. 100, no. 1–2, pp. 100–107, Aug. 2005, doi: 10.1016/j.jep.2005.07.001.

[99] M. Suwalsky, J. Duguet, and H. Speisky, "An In Vitro Study of the Antioxidant and Antihemolytic Properties of Buddleja globosa (Matico)," *J Membr Biol*, Apr. 2017, doi: 10.1007/s00232-017-9955-0.

[100] M. E. Letelier *et al.*, "DPPH and oxygen free radicals as pro-oxidant of biomolecules," *Toxicology in Vitro*, vol. 22, no. 2, pp. 279–286, Mar. 2008, doi: 10.1016/j.tiv.2007.08.002.

[101] M. E. Letelier, P. A. Iturra-montecinos, and C. A. Gallardo-garrido, "Herbal extracts differentially inhibit oxidative effects caused by the biotransformation of nifurtimox , nitrofurantoin and acetaminophen on rat liver microsomes," *Bol Latinoam Caribe Plantas Med Aromat*, vol. 16, no. 2, pp. 88–98, 2017.

[102] E. R. Carmona, N. Benito, T. Plaza, and G. Recio-Sánchez, "Green synthesis of silver nanoparticles by using leaf extracts from the endemic Buddleja globosa hope," *Green Chem Lett Rev*, vol. 10, no. 4, pp. 250–256, 2017, doi: 10.1080/17518253.2017.1360400.

[103] J. Vera *et al.*, "Antioxidant Activity as an Indicator of the Efficiency of Plant Extract-Mediated Synthesis of Zinc Oxide Nanoparticles," *Antioxidants*, vol. 12, no. 4, 2023, doi: 10.3390/antiox12040784.

[104] G. Darrow, *The Strawberry: History, Breeding, and Physiology*, 1 Ed. New York, 1966.

[105] C. E. Finn, J. B. Retamales, G. A. Lobos, and J. F. Hancock, "The chilean strawberry (Fragaria chiloensis): Over 1000 years of domestication," *HortScience*, vol. 48, no. 4, pp. 418–421, 2013.

[106] C. K. Weebadde *et al.*, "Using a linkage mapping approach to identify QTL for day-neutrality in the octoploid strawberry," *Plant Breeding*, vol. 127, no. 1, pp. 94–101, Oct. 2007, doi: 10.1111/j.1439-0523.2007.01430.x.

[107] R. A. Fadri, S. Salvia, R. Novita, Y. Muchrida, S. Kembaryanti Putri, and F. Violalita, "Phenolics Total and Antioxidant Activity of Strawberry (Fragaria chiloensis)," *Int J Adv Sci Eng Inf Technol*, vol. 5, no. 6, p. 392, 2015, doi: 10.18517/ijaseit.5.6.591.

[108] M. J. Simirgiotis, C. Theoduloz, P. D. S. Caligari, and G. Schmeda-Hirschmann, "Comparison of phenolic composition and antioxidant properties of two native Chilean and one domestic strawberry genotypes," *Food Chem*, vol. 113, no. 2, pp. 377–385, Mar. 2009, doi: 10.1016/j.foodchem.2008.07.043.

[109] S. Skrovankova, D. Sumczynski, J. Mlcek, T. Jurikova, and J. Sochor, "Bioactive Compounds and Antioxidant Activity in Different Types of Berries," *Int J Mol Sci*, vol. 16, no. 10, pp. 24673–24706, Oct. 2015, doi: 10.3390/ijms161024673.

[110] F. Noriega, C. Mardones, S. Fischer, C. Garciá-Viguera, D. A. Moreno, and M. D. López, “Seasonal changes in white strawberry: Effect on aroma, phenolic compounds and its biological activity,” *J Berry Res*, vol. 11, no. 1, pp. 103–118, 2021, doi: 10.3233/JBR-200585.

[111] A. Salvatierra, P. Pimentel, M. A. Moya-León, and R. Herrera, “Biosynthesis of flavonoids in achenes of Fragaria chiloensis ssp. chiloensis,” *Bol Latinoam Caribe Plantas Med Aromat*, vol. 13, no. 4, pp. 406–414, Dec. 2004.

[112] L. Morales-Quintana and P. Ramos, “Chilean strawberry (Fragaria chiloensis): An integrative and comprehensive review,” *Food Research International*, vol. 119, no. October 2018, pp. 769–776, 2019, doi: 10.1016/j.foodres.2018.10.059.

[113] M. Reyes-Farias *et al*., “Chilean Native Fruit Extracts Inhibit Inflammation Linked to the Pathogenic Interaction Between Adipocytes and Macrophages,” *J Med Food*, vol. 18, no. 5, pp. 601–608, May 2014, doi: 10.1089/jmf.2014.0031.

[114] S. Thomas-Valdés, C. Theoduloz, F. Jiménez-Aspee, and G. Schmeda-Hirschmann, “Effect of simulated gastrointestinal digestion on polyphenols and bioactivity of the native Chilean red strawberry (Fragaria chiloensis ssp. chiloensis f. patagonica),” *Food Research International*, vol. 123, no. January, pp. 106–114, 2019, doi: 10.1016/j.foodres.2019.04.039.

[115] E. Genskowsky, L. A. Puente, J. A. Pérez-Álvarez, J. Fernández-López, L. A. Muñoz, and M. Viuda-Martos, “Determination of polyphenolic profile, antioxidant activity and antibacterial properties of maqui [Aristotelia chilensis (Molina) Stuntz] a Chilean blackberry,” *J Sci Food Agric*, vol. 96, no. December 2015, pp. 4235–4242, 2016, doi: 10.1002/jsfa.7628.

[116] A. M. Connor, J. J. Luby, J. F. Hancock, S. Berkheimer, and E. J. Hanson, “Changes in Fruit Antioxidant Activity among Blueberry Cultivars during Cold-Temperature Storage,” *J Agric Food Chem*, vol. 50, no. 4, pp. 893–898, Feb. 2002, doi: 10.1021/jf011212y.

[117] I. M. Heinonen, A. S. Meyer, and E. N. Frankel, “Antioxidant Activity of Berry Phenolics on Human Low-Density Lipoprotein and Liposome Oxidation,” *J Agric Food Chem*, vol. 46, no. 10, pp. 4107–4112, Oct. 1998, doi: 10.1021/jf980181c.

[118] P. Morazzoli and E. Bombardelli, “Vaccinium myrtillus L.,” *Fitoterapia*, vol. 67, no. 1, pp. 3–29, 1996.

[119] J. R. Sparrow *et al*., “A2E-epoxides Damage DNA in Retinal Pigment Epithelial Cells,” *Journal of Biological Chemistry*, vol. 278, no. 20, pp. 18207–18213, May 2003, doi: 10.1074/jbc.M300457200.

[120] N. Katsube, K. Iwashita, T. Tsushida, K. Yamaki, and M. Kobori, “Induction of Apoptosis in Cancer Cells by Bilberry (Vaccinium myrtillus) and the Anthocyanins,” *J Agric Food Chem*, vol. 51, no. 1, pp. 68–75, Jan. 2003, doi: 10.1021/jf025781x.

[121] C. López de Dicastillo, F. Rodríguez, A. Guarda, and M. J. Galotto, “Antioxidant films based on cross-linked methyl cellulose and native Chilean berry for food packaging applications,” *Carbohydr Polym*, vol. 136, pp. 1052–1060, Jan. 2016, doi: 10.1016/j.carbpol.2015.10.013.

[122] K. A. Crisóstomo-Ayala *et al*., “Comparative Study of Metabolomic Profile and Antioxidant Content of Adult and In Vitro Leaves of Aristotelia chilensis,” *Plants*, vol. 11, no. 1, p. 37, Dec. 2021, doi: 10.3390/plants11010037.

[123] C. Céspedes, J. Jakupovic, M. Silva, and W. Watson, “Indole alkaloids from Aristotelia chilensis,” *Phytochemistry*, vol. 29, no. 4, pp. 1354–1356, Jan. 1990, doi: 10.1016/0031-9422(90)85469-V.

[124] He, S. Valcic, B. N. Timmermann, and G. Montenegro, “Indole Alkaloids from Aristotelia chilensis (Mol.) Stuntz,” *International Journal of Pharmacognosy*, vol. 35, no. 3, p. S. 215-217, 1997.

[125] K. Rodríguez *et al*., “Changes in bioactive components and antioxidant capacity of maqui, Aristotelia chilensis [Mol] Stuntz, berries during drying,” *LWT - Food Science and Technology*, vol. 65, pp. 537–542, Jan. 2016, doi: 10.1016/j.lwt.2015.08.050.

[126] H. F. Chiu, K. Venkatakrishnan, O. Golovinskaia, and C. K. Wang, “Gastroprotective effects of polyphenols against various gastro-intestinal disorders: A mini-review with special focus on clinical evidence,” *Molecules*, vol. 26, no. 7, 2021, doi: 10.3390/molecules26072090.

[127] O. Golovinskaia and C. K. Wang, “Review of functional and pharmacological activities of berries,” *Molecules*, vol. 26, no. 13, 2021, doi: 10.3390/molecules26133904.

[128] O. Golovinskaia and C. K. Wang, “The hypoglycemic potential of phenolics from functional foods and their mechanisms,” *Food Science and Human Wellness*, vol. 12, no. 4, pp. 986–1007, 2023, doi: 10.1016/j.fshw.2022.10.020.

[129] O. Muñoz and F. Ramos, “Quantitative analysis of phytosterols in Aristotelia chilensis (Maqui) leaves using GC/MS,” *Int Food Res J*, vol. 23, no. 2, pp. 822–826, 2016.

[130] C. L. Céspedes, M. El-Hafidi, N. Pavon, and J. Alarcon, “Antioxidant and cardioprotective activities of phenolic extracts from fruits of Chilean blackberry Aristotelia chilensis (Elaeocarpaceae), Maqui,” *Food Chem*, vol. 107, no. 2, pp. 820–829, Mar. 2008, doi: 10.1016/j.foodchem.2007.08.092.

[131] C. T. da Costa, D. Horton, and S. A. Margolis, “Analysis of anthocyanins in foods by liquid chromatography, liquid chromatography–mass spectrometry and capillary electrophoresis,” *J Chromatogr A*, vol. 881, no. 1–2, pp. 403–410, Jun. 2000, doi: 10.1016/S0021-9673(00)00328-9.

[132] M. M. Giusti, L. E. Rodrı, D. Griffin, and R. E. Wrolstad, “Electrospray and Tandem Mass Spectroscopy As Tools for Anthocyanin Characterization,” *J. Agric. Food. Chem.*, vol. 47, no. 11, pp. 4657–4664, 1999, doi: 10.1021/jf981242+.

[133] J. E. Brauch, M. Buchweitz, R. M. Schweiggert, and R. Carle, “Detailed analyses of fresh and dried maqui (Aristotelia chilensis (Mol.) Stuntz) berries and juice,” *Food Chem*, vol. 190, pp. 308–316, 2016, doi: 10.1016/j.foodchem.2015.05.097.

[134] A. Gironés-Vilaplana, P. Valentão, P. B. Andrade, F. Ferreres, D. A. Moreno, and C. García-Viguera, “Phytochemical profile of a blend of black chokeberry and lemon juice with cholinesterase inhibitory effect and antioxidant potential,” *Food Chem*, vol. 134, no. 4, pp. 2090–2096, Oct. 2012, doi: 10.1016/j.foodchem.2012.04.010.

[135] A. Ruiz, E. Pastene, C. Vergara, D. Von Baer, M. Avello, and C. Mardones, “Hydroxycinnamic acid derivatives and flavonol profiles of maqui (Aristotelia chilensis) fruits,” *Journal of the Chilean Chemical Society*, vol. 61, no. 1, pp. 2792–2796, 2016, doi: 10.4067/S0717-97072016000100010.

[136] J. E. Brauch, L. Reuter, J. Conrad, H. Vogel, R. M. Schweiggert, and R. Carle, “Characterization of anthocyanins in novel Chilean maqui berry clones by HPLC–DAD–ESI/MSn and NMR-spectroscopy,” *Journal of Food Composition and Analysis*, vol. 58, pp. 16–22, May 2017, doi: 10.1016/j.jfca.2017.01.003.

[137] L. E. Rojo *et al*., “In vitro and in vivo anti-diabetic effects of anthocyanins from Maqui Berry (Aristotelia chilensis),” *Food Chem*, vol. 131, no. 2, pp. 387–396, Mar. 2012, doi: 10.1016/j.foodchem.2011.08.066.

[138] I. Quispe-Fuentes, A. Vega-Gálvez, and V. Campos-Requena, “Antioxidant Compound Extraction from Maqui (Aristotelia chilensis [Mol] Stuntz) Berries: Optimization by Response Surface Methodology,” *Antioxidants*, vol. 6, no. 1, p. 10, Feb. 2017, doi: 10.3390/antiox6010010.

[139] R. Lucas-Gonzalez, S. Navarro-Coves, J. A. Pérez-Álvarez, J. Fernández-López, L. A. Muñoz, and M. Viuda-Martos, “Assessment of polyphenolic profile stability and changes in the antioxidant potential of maqui berry (Aristotelia chilensis (Molina) Stuntz) during in vitro gastrointestinal digestion,” *Ind Crops Prod*, vol. 94, pp. 774–782, Dec. 2016, doi: 10.1016/j.indcrop.2016.09.057.

[140] D. Hernández-Prieto, P. S. Fernández, V. Agulló, C. García-Viguera, and J. A. Egea, "Bioactive Compounds in Plasma as a Function of Sex and Sweetener Resulting from a Maqui-Lemon Beverage Consumption Using Statistical and Machine Learning Techniques," *Int J Mol Sci*, vol. 24, no. 3, p. 2140, Jan. 2023, doi: 10.3390/ijms24032140.

[141] G. Montenegro, *Chile , nuestra flora útil : guía de plantas de uso apícola , en medicina folklórica , artesanal y ornamental*. Santiago, 2000.

[142] J. Zin and C. Weiss, *La salud por medio de las plantas medicinales*, Novena. Santiago, Chile.: Editorial Don Bosco, 2006.

[143] M. Avello, E. Pastene, A. Barriga, M. Bittner, E. Ruiz, and J. Becerra, "Chemical properties and assessment of the antioxidant capacity of leaf extracts from populations of ugni molinae growing in continental Chile and in Juan fernandez archipelago," *International Journal of Pharmacognosy and Phytochemical Research*, vol. 6, no. 4, pp. 746–752, 2014.

[144] M. A. Avello, E. R. Pastene, E. D. Bustos, M. L. Bittner, and J. A. Becerra, "Variation in phenolic compounds of Ugni molinae populations and their potential use as antioxidant supplement," *Revista Brasileira de Farmacognosia*, vol. 23, no. 1, pp. 44–50, Jan. 2013, doi: 10.1590/S0102-695X2012005000122.

[145] L. E. Goity *et al.*, "An HPLC-UV and HPLC-ESI-MS based method for identification of anti- inflammatory triterpenoids from the extracts of Ugni molinae," *Bol Latinoam Caribe Plantas Med Aromat*, vol. 12, no. 1, pp. 108–116, 2013.

[146] L. E. Goity *et al.*, "An HPLC-UV and HPLC-ESI-MS based method for identification of anti- inflammatory triterpenoids from the extracts of Ugni molinae," *Bol Latinoam Caribe Plantas Med Aromat*, vol. 12, no. 1, pp. 108–116, 2013.

[147] C. Shene, A. K. Reyes, M. Villarroel, J. Sineiro, M. Pinelo, and M. Rubilar, "Plant location and extraction procedure strongly alter the antimicrobial activity of murta extracts," *European Food Research and Technology*, vol. 228, no. 3, pp. 467–475, Jan. 2009, doi: 10.1007/s00217-008-0954-3.

[148] L. Puente-Díaz, K. Ah-Hen, A. Vega-Gálvez, R. Lemus-Mondaca, and K. Di Scala, "Combined Infrared-Convective Drying of Murta (Ugni molinae Turcz) Berries: Kinetic Modeling and Quality Assessment," *Drying Technology*, vol. 31, no. 3, pp. 329–338, Feb. 2013, doi: 10.1080/07373937.2012.736113.

[149] M. Reyes-Farias *et al.*, "Extracts of Chilean native fruits inhibit oxidative stress, inflammation and insulin-resistance linked to the pathogenic interaction between adipocytes and macrophages," *J Funct Foods*, vol. 27, pp. 69–83, Dec. 2016, doi: 10.1016/j.jff.2016.08.052.

[150] A. Reyes, V. Bubnovich, R. Bustos, M. Vásquez, R. Vega, and E. Scheuermann, "Comparative Study of Different Process Conditions of Freeze Drying of 'Murtilla' Berry," *Drying Technology*, vol. 28, no. 12, pp. 1416–1425, Nov. 2010, doi: 10.1080/07373937.2010.482687.

[151] A. Reyes, A. Evseev, A. Mahn, V. Bubnovich, R. Bustos, and E. Scheuermann, "Effect of operating conditions in freeze-drying on the nutritional properties of blueberries," *Int J Food Sci Nutr*, vol. 62, no. 3, pp. 303–306, May 2011, doi: 10.3109/09637486.2010.534078.

[152] J. López, A. Vega-Gálvez, C. Bilbao-Sainz, B.-S. Chiou, E. Uribe, and I. Quispe-Fuentes, "Influence of vacuum drying temperature on: Physico-chemical composition and antioxidant properties of murta berries," *J Food Process Eng*, no. March, p. e12569, Apr. 2017, doi: 10.1111/jfpe.12569.

[153] T. R. Augusto-Obara, F. Pirce, E. Scheuermann, M. H. F. Spoto, and T. M. F. S. Vieira, "Antioxidant activity and sensory analysis of murtilla (Ugni molinae Turcz.) fruit extracts in an oil model system," *Grasas y Aceites*, vol. 68, no. 1, p. 183, Mar. 2017, doi: 10.3989/gya.0810162.

[154] L. S. Gómez-Pérez, N. Moraga, K. S. Ah-Hen, A. Rodríguez, and A. Vega-Gálvez, "Dietary fibre in processed murta (Ugni molinae Turcz) berries: bioactive components and antioxidant capacity," *J Food Sci Technol*, vol. 59, no. 8, pp. 3093–3101, Aug. 2022, doi: 10.1007/s13197-022-05416-1.

[155] S. Srivastava, M. Srivastava, A. Misra, G. Pandey, and A. Rawa, "Review article : A REVIEW ON BIOLOGICAL AND CHEMICAL DIVERSITY," *EXCLI J*, no. 14, pp. 247–267, 2015.

[156] D. Alarcón, M. Paredes, D. Ramos, K. González, R. Díaz, and D. Núñez, "Los extractos acuoso y metanólico de Berberis darwinii H. (Berberidaceae) inhiben respuestas celulares innatas en monocitos humanos tratados in vitro," *Bol Latinoam Caribe Plantas Med Aromat*, vol. 13, no. 1, pp. 81–91, 2014.

[157] J. L. Martínez, R. Torres, and M. A. Morales, "Hypotensive effect of O-methylisothalicberine, a bisbenzylisoquinoline alkaloid isolated fromBerberis chilensis on normotensive rats," *Phytotherapy Research*, vol. 11, no. 3, pp. 246–248, May 1997, doi: 10.1002/(SICI)1099-1573(199705)11:3<246::AID-PTR62>3.0.CO;2-J.

[158] M. A. Morales, E. González, R. Torres, and J. L. Martínez, "Cardiodepressor effects of 7-O-demethylisothalicberine, bisbenzylisoquinoline alkaloid isolated from Berberis chilensis.," *Arch Med Res*, vol. 24, no. 2, pp. 177–181, 1993.

[159] R. D. Enriz and M. L. Freile, "Structure-activity relationship of berberine and derivatives acting as antifungal compounds," *Anales de la Asociación Química Argentina*, vol. 94, no. 1–3, pp. 113–119, 2006.

[160] M. L. Freile *et al.*, "Antimicrobial activity of aqueous extracts and of berberine isolated from Berberis heterophylla," *Fitoterapia*, vol. 74, no. 7–8, pp. 702–705, Dec. 2003, doi: 10.1016/S0367-326X(03)00156-4.

[161] S. I. Pitta-Alvarez, F. Medina-Bolivar, M. A. Alvarez, A. A. Scambatto, and P. L. Marconi, "In vitro shoot culture and antimicrobial activity of Berberis buxifolia Lam," *In Vitro Cellular & Developmental Biology - Plant*, vol. 44, no. 6, pp. 502–507, Dec. 2008, doi: 10.1007/s11627-008-9136-z.

[162] J. E. Ramirez, R. Zambrano, B. Sep??lveda, E. J. Kennelly, and M. J. Simirgiotis, "Anthocyanins and antioxidant capacities of six Chilean berries by HPLC-HR-ESI-ToF-MS," *Food Chem*, vol. 176, pp. 106–114, 2015, doi: 10.1016/j.foodchem.2014.12.039.

[163] L. Manosalva, A. Mutis, A. Urzúa, V. Fajardo, and A. Quiroz, "Antibacterial Activity of Alkaloid Fractions from Berberis microphylla G. Forst and Study of Synergism with Ampicillin and Cephalothin," *Molecules*, vol. 21, no. 1, p. 76, Jan. 2016, doi: 10.3390/molecules21010076.

[164] S. Radice and M. E. Arena, "Environmental effect on the leaf morphology and anatomy of Berberis microphylla G. Forst," *International Journal of Plant Biology*, vol. 6, no. 1, pp. 1–7, Sep. 2015, doi: 10.4081/pb.2015.5677.

[165] L. R. Landrum, "Revision of Berberis (Berberidaceae) in Chile and adjacent southern Argentina," *Ann. Missouri Bot. Gard*, vol. 86, no. 4, pp. 793–834, 1999.