
Native Chilean Fruits and the Effects of Their Functional Compounds on Human Health

Elizabeth M. Ulloa-Inostroza, Eric G. Ulloa-Inostroza,
Miren Alberdi, Daniela Peña-Sanhueza,
Jorge González-Villagra, Laura Jaakola and
Marjorie Reyes-Díaz

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Abstract

In recent years, there has been great interest in the nutraceutical compounds of fruits from native Chilean plant species. In this context, fruits of *Amomyrtus meli* (Meli), *Aristotelia chilensis* (Maqui), *Berberis microphylla* (Calafate), *Luma apiculata* (Arrayán), *Luma chequén* (Chequén), and *Ugni molinae* (Murtilla) growing predominantly in Chilean forests have been studied. This chapter has compiled the existing information about antioxidant activity and antioxidant compound contents of the above mentioned fruit species and their association with the prevention of pathophysiological disorders in humans, such as inflammation, diabetes, and cardiovascular diseases. Results show that the antioxidant compounds of these species, particularly anthocyanins, decrease inflammation as well as the risk of diabetes and cardiovascular diseases. Therefore, consumption of these fruits is a good alternative for preventing cardiovascular and age-related diseases and pathophysiological disorders.

Keywords: *Amomyrtus meli*, *Aristotelia chilensis*, arrayán, antioxidant, *Berberis microphylla*, calafate, cardiovascular, carcinogenesis, chequén, diabetes, inflammatory, *Luma apiculata*, *Luma chequén*, maqui, meli, murtilla, phenolic compounds, *Ugni molinae*

1. Introduction

Chile is a South American country bordered by Perú to the north, Bolivia to the northeast, and Argentina to the east. The continental Chilean territory is a long, narrow strip of land between the Andes in the east and the Pacific Ocean in the west. Its island territories include the Pacific

islands of Juan Fernández, Salas y Gómez, Desventuradas, and Pascua and Easter Island in Oceania [1, 2]. Due to its long surface and geographical location, Chile has a large range of different climates from tropical to polar, creating great diversity in its ecosystems and richness in its biodiversity [1–4]. This promotes better use of natural resources for improving the bioeconomy of the country [1, 3]. Traditionally, native Chilean fruits have been used as medicine by Chilean ethnic groups [5]. Currently, studies into native Chilean fruits have focused on identifying and defining their key compounds with medicinal effects [6]. Native Chilean species with edible fruits include woody or shrub forest species belonging to the Elaeocarpaceae, Berberidaceae, and particularly Myrtaceae families (Table 1). These families are distributed from Illapel to Tierra del Fuego (Figure 1) and are species-rich in antioxidant and nutraceutical compounds with benefits to human health, including *Amomyrtus meli* (Meli) (Figure 2), *Aristotelia chilensis* (Maqui) (Figure 3), *Berberis microphylla* (Calafate) (Figure 4), *Luma apiculata* (Arrayán) (Figure 5), *Luma chequén* (Chequén) (Figure 6), and *Ugni molinae* (Murtilla) (Figure 7) [3, 7–11]. These species inhabit the Valdivian Evergreen Forest (Bosque siempreverde Valdiviano) and the Evergreen Patagonian Forest (Bosque siempreverde Patagónico) together with other Chilean forest species that have not been domesticated. Interestingly, Murtilla is the most domesticated among them [10, 12–16].

Scientific name of plant species	Common name	Family	References
<i>Amomyrtus meli</i> (Phil.) D. Legrand & Kausel.	Meli	Myrtaceae	[39, 54]
<i>Aristotelia chilensis</i> (Mol.) Stuntz.	Maqui	Elaeocarpaceae	
<i>Berberis microphylla</i> G. Forst.	Calafate	Berberidaceae	
<i>Luma apiculata</i> (DC.) Burret.	Arrayán, Arrayán rojo, Luma, Palo colorado, Temu	Myrtaceae	
<i>Luma chequen</i> (Mol.) A. Gray.	Arrayán Blanco, Chequén	Myrtaceae	
<i>Ugni molinae</i> Turcz.	Murtilla	Myrtaceae	

Table 1. Scientific and common name as well as families of the native Chilean fruits.

Scalbert et al. [17] and Lila et al. [18] reported a relationship between consumption of fruits with high antioxidant contents and a reduction in oxidative stress in humans. The richness and abundance of enzymatic and nonenzymatic antioxidants in plant species decrease the oxidative damage, helping to inhibit the formation of free radicals by several mechanisms: (1) inhibiting the initiation of the peroxidation, (2) preventing formation of reactive oxygen species (ROS), and (3) breaking the autoxidation chain reaction in humans [19–22]. ROS are normally produced in humans but are exacerbated under exogenous stresses (ozone, cigarette smoking, air pollutants, etc.) [23–27]. Chemical effectiveness of antioxidants against ROS is due to the protection of biomolecules such as lipids, proteins, and carbohydrates to prevent damage by oxidative stress in biomembranes. For this reason, it is very important that people consume antioxidant-rich fruits or foods to decrease ROS [28]. The human diseases associated with oxidative stress are the inflammatory process, cardiovascular disorders, and carcinogenesis (gastric and colorectal) [29–32]. Therefore, fruits with a high antioxidant power are of great benefit in disease prevention related with the inflammatory process and in particular associated with oxidative stress [6, 33–35].

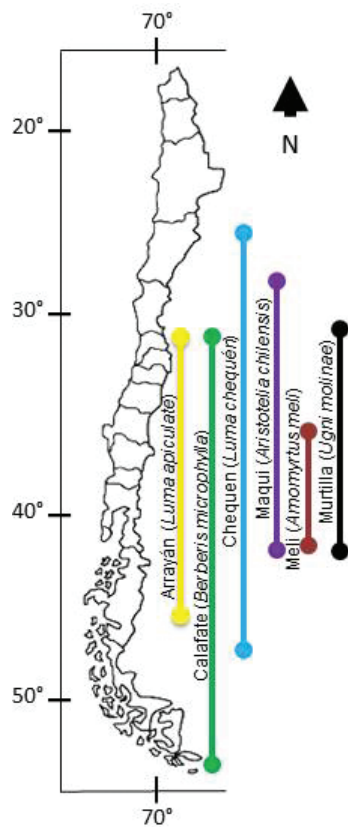


Figure 1. Geographical distribution of native species in the forests of continental Chile.

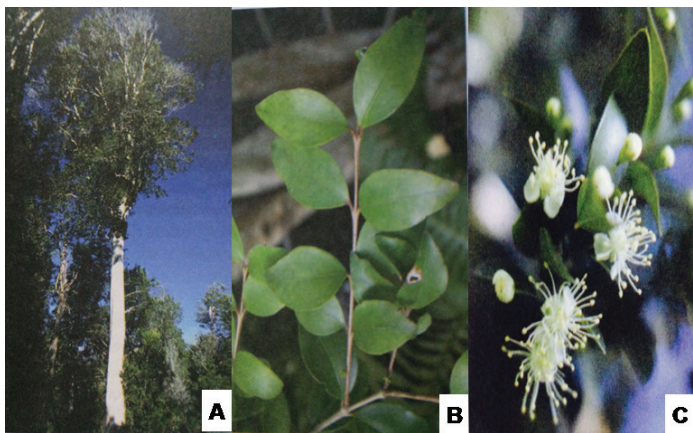


Figure 2. Pictures of *Amomyrtus meli* (Meli): tree (A), leaves (B), and flowers (C). Extracted from Donoso [40].

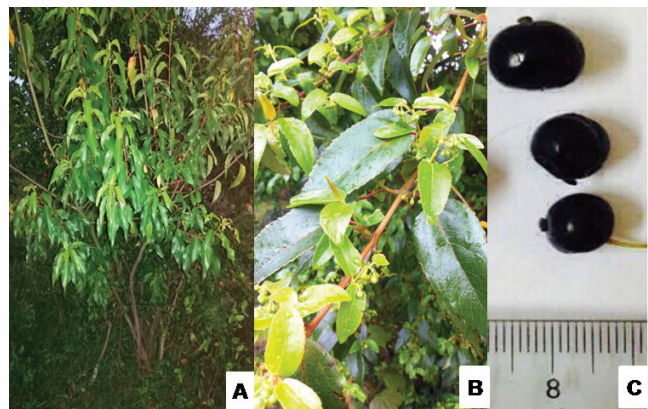


Figure 3. Pictures of *Aristotelia chilensis* (Maqui): tree (A), leaves (B), and fruits (C).

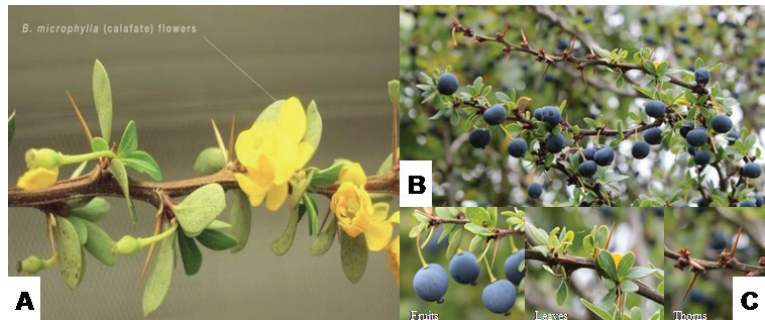


Figure 4. Pictures of *Berberis microphylla* (Calafate): flowers (A), fruits (B) and composed pictures of fruits, leaves, and thorns (C).

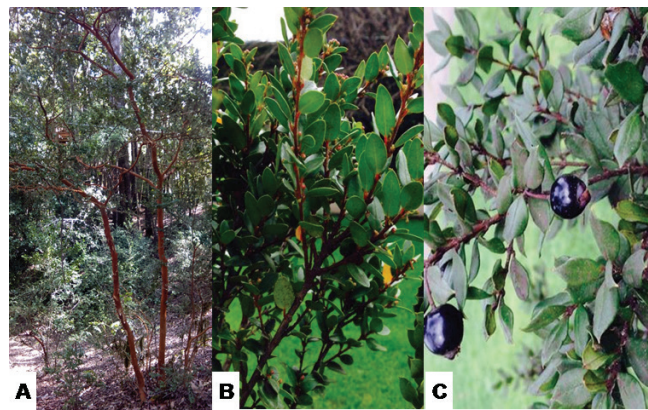


Figure 5. Pictures of *Luma apiculata* (Arrayán): tree (A), leaves (B), and fruits (C). The picture was replaced by an our picture.

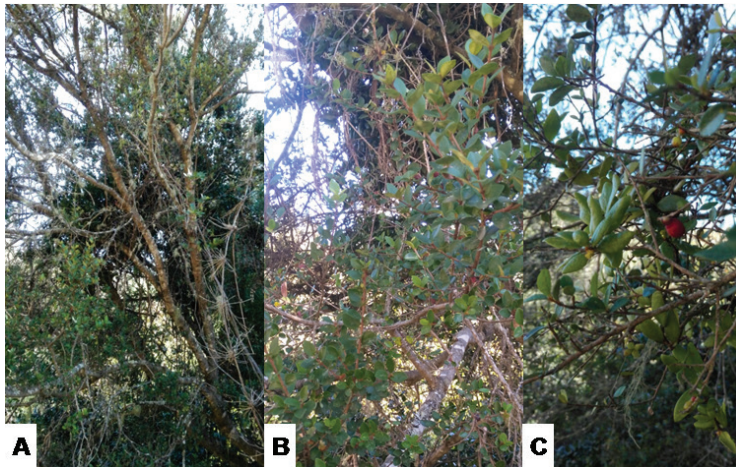


Figure 6. Pictures of *Luma chequen* (Chequén): tree (A), leaves (B), and immature fruits (C).

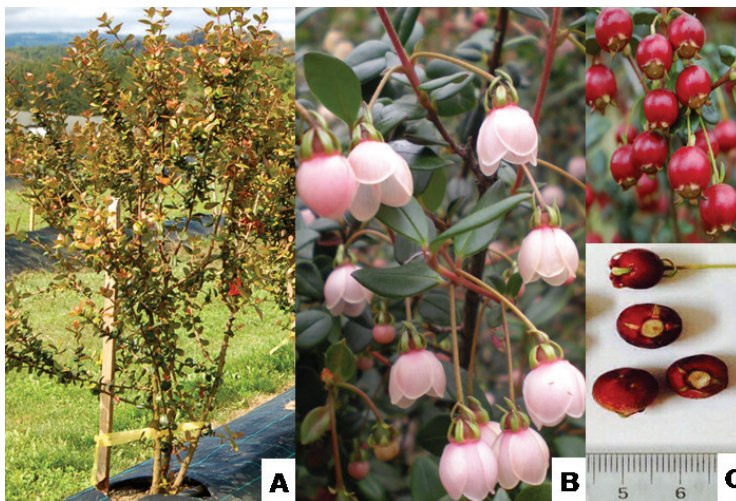


Figure 7. Pictures of *Ugni molinae* (Murtilla): tree (A), flowers (B), and fruits (C).

Regarding native fruits rich in antioxidants and other bioactive compounds, it is important to detect the quality and quantity of the compounds responsible for the health beneficial properties [36–38]. In this context, the aim of this review is to associate the main bioactive compounds, antioxidant activity, and content of individual phenolic compounds of some native Chilean fruits such as Arrayán (Figure 5), Calafate (Figure 4), Chequén (Figure 6), Maqui (Figure 3), Meli (Figure 2), and Murtilla (Figure 7) with the prevention of diseases and pathophysiological disorders in humans.

2. Morphological characterization, geographical distribution, and ethnobotany of native Chilean fruits

2.1. *A. meli* (Meli) (Phil.) D. Legrand & Kausel

A. meli is a deciduous tree endemic to Chile, reaching a height up to 20 m (**Figure 2A**). It has a very distinctive white trunk, which makes it unmistakable among the species of Chilean trees [39]. It grows mostly on moist and shaded sites from the Arauco to Chiloé Regions (**Figure 1**) in the coastal rainforest, growing on the banks of waterways or under the canopy of other larger species [40]. No conservation problems have been reported for this species, although it is present in a few protected areas such as Chiloé National Park, the Valdivian Coast Reserve, and Oncol Park [39]. Despite its palatability, its fruits are not consumed because they have been reported to cause headaches. The infusion of its leaves is recommended as medicinal use for hypertension (**Figure 2B**) [14, 39]. It has great ornamental potential due to its abundant and very fragrant flowering (**Figure 2C**).

2.2. *A. chilensis* (Maqui) (Mol.) Stuntz

A. chilensis is an evergreen species endemic to Chile (**Figure 3A**), and it is distributed from Illapel (Coquimbo Region) to Chiloé (Los Lagos Region) (**Figure 1**) [37]. It grows naturally, forming wild populations named “macales” and can protect against erosion, since it grows rapidly in abandoned, burned, or overexploited soils [41]. The bright green Maqui leaves are oval-lanceolate with a serrated edge (**Figure 3B**) [42]. The fruits are small, purple bright berries about 5 mm of diameter (**Figure 3C**), with two to five small seeds inside and are eaten fresh, in juice or in jam, and also used as food coloring and in wine-making [42, 43]. Maqui fruits have been of great interest to consumers for their high antioxidant activity, mainly due to phenolic compounds (**Figure 3C**) [44–46], which means this species has been considered a “superfruit” [47].

2.3. *B. microphylla* (Calafate) G. Forst

B. microphylla, commonly called Calafate, is a native Chilean plant species belonging to the Berberidaceae family (**Table 1**) [10, 15]. It is an evergreen shrub 2–3 m high with thorns and single yellow flowers (**Figure 4A**). Its fruit (barberry) is a dark blue-purple berry 7–11 mm in size (**Figure 4B** and **C**) [15, 48, 49]. Berberis genus incorporate among 20–60 species in South America, and the majority is commonly known as Michay or Calafate [50, 51]. In Chile, Calafate is distributed from Curicó to Tierra del Fuego at different altitudes and grows under a wide range of ecological conditions (**Figure 1**) [15, 48, 52]. This species is not cultivated and grows in the wild or in small gardens. Its fruits are used to prepare jam, juice, and wine [10, 15, 48, 50].

2.4. *Luma apiculata* (Arrayán) (DC) Burret

L. apiculata or Arrayán is an evergreen tree of the Valdivian Evergreen Forest (**Figure 5A**). Its bark is smooth reddish with whitish parts, reaching heights from 12 to 15 m tall with a crooked trunk around 50 cm in diameter (**Figure 5A**) [14, 40, 53]. The flowers are hermaphrodites and axillary arranged in groups of three or five, which form a berry, a small, black edible fruit

(1.3–1.5 cm in diameter) (**Figure 5C**) [39, 51]. It is distributed in Chile from the Valparaíso to Aysén Regions (**Figure 1**) on lakeshores and riverbeds and on very moist soils. Trees of this species are conserved in various National Parks, including La Campana, Radal Siete Tazas, Laguna del Laja, Huerquehue, Puyehue, and Chiloé. Arrayán roots have medicinal uses as an anti-hemorrhagic and astringent, while the bark is used to treat herpes and ulcers, and the leaves (**Figure 5B**) to heal wounds, and treat stomach disorders [55].

2.5. *Luma chequen* (Chequén) (Mol.) A. Gray

The Chequén is an endemic tree of the Andean forests in Chile (**Figure 6A**). It is distributed from Coquimbo to Capitán Prat (**Figure 1**) [39]. It grows only in areas of high humidity, on the banks of streams, and in gulches [39]. It is a medium-sized branched shrub, which reaches 9 m in height, with grayish brown bark, and the whole plant gives off a pleasant aroma (**Figure 6A**) [39]. The leaves are oval, wide, and short (**Figure 6B**). The berry fruits are edible and dark purple 1 cm in diameter, ripening in early autumn (**Figure 6C**) [14, 39].

2.6. *Ugni molinae* (Murtilla) Turcz

Natural habitats of Murtilla are forests and coastal mountains from Valparaíso to Aysén (**Figure 1**). It is an evergreen shrub from 1 to 2 m tall (**Figure 7A**) [56, 57]. The dark green leaves are lanceolate, and the flowers are hermaphrodite (**Figure 7B**) [56]. The fruits are bright red globose berries 5–15 mm in diameter with a sweet taste and a strong aroma (**Figure 7C**) [56, 58]. Murtilla is adapted to most soils and is resistant to drought, wind, and cold, but not frost [59]. The traditional uses are for jams, juices, chocolates, and liqueur production (enmurtado or enmutillado).

3. Effect of Chilean fruits on diseases and pathophysiological disorders: beneficial effects on human health

3.1. Bioactive compounds in native Chilean fruits

Native Chilean fruits are naturally rich in phenolic compounds beneficial to human health (**Tables 2 and 3**) [8, 14, 48]. Phenolic compounds are plant secondary metabolites with bioactive properties and are generally involved in the defense against stress conditions in plants [60, 61]. They can be generally characterized by astringency, color, flavor, odor, and oxidative stability [62, 63]. In recent years, the phenolic compounds of wild or domesticated Arrayán, Chequén, Maqui, Meli, and Murtilla have been studied, with the results highlighting the high antioxidant activity of their leaves and fruits [8, 14–16, 48]. The main phenolic compounds in these fruits can be divided into phenolic acids, flavonoids, flavanols, and anthocyanins [63, 64] (**Tables 2 and 3**). Ruiz et al. [48] performed a comparison using total antioxidant activity and Trolox equivalent antioxidant capacity (TEAC) methods among edible fruits of Calafate, Maqui, and Murtilla, showing that Maqui and Calafate had a higher antioxidant activity with 88.1 and 74.5 Trolox equivalent (TE) g⁻¹ of FW, respectively, followed by Murtilla with 11.7 TE g⁻¹ FW. Afterward, this was confirmed by Dai and Mumper [65], who determined antioxidant activity in Maqui and Murtilla fruits with one of the most

commonly used methods, that is, the 2,2-diphenylpicrylhydrazyl (DPPH) assay. The antioxidant activity was higher in Maqui (399.8) than in Murtilla (82.9) in milligrams of crude extract per Liter⁻¹ (mg of crude extract L⁻¹). This method is based on the measurement of the antioxidant compounds able to scavenge the stable free radical DPPH. It is a simple, rapid, and inexpensive method [66]. Usually, the results are expressed as milligrams of a sample that bleached 50% of the DPPH solution (IC₅₀) [67]. Therefore, low IC₅₀ values show a high antioxidant activity. In this antioxidant assay, Brand-Williams et al. [68] reported that to reach IC₅₀ only 0.0016 g L⁻¹ of Maqui fruit is necessary; meanwhile, for “Blueberries” (*Vaccinium corymbosum*), “Strawberries” (*Fragaria ananassa*), and “Raspberries” (*Rubus idaeus*) an average of 0.03 g L⁻¹ of fruits is needed. The result of IC₅₀ for Maqui fruits was confirmed by Fredes et al. [69] and Céspedes et al. [70], who reported IC₅₀ values of 0.0012 and 0.0019 g L⁻¹ by DPPH assay, respectively. This means that Maqui fruits exhibited the highest antioxidant activity compared with other berries cultivated in Chile. Additionally, Dai and Mumper [65] compared phenolic compounds of leaves and fruits, showing that in Maqui leaves, concentrations were 200% and in Murtilla, 50% higher than in other fruits. Another commonly used method to determine total antioxidants is the oxygen-radical absorbing capacity (ORAC), which measures the antioxidant values as TE and includes both inhibition time and extent of oxidation inhibition [71, 72]. With this method, Prior et al. [73] reported that fruits of wild Calafate have 25 and 150% higher antioxidant activity than Maqui and Murtilla, respectively.

Phenolic compounds profile	Arrayán (<i>L. apiculata</i>)	Calafate (<i>B. microphylla</i>)	Chequén (<i>L. chequen</i>)	Maqui (<i>A. chilensis</i>)	Meli (<i>A. meli</i>)	Murtilla (<i>U. molinae</i>)
Caffeic acid	ND	+	ND	ND	ND	ND
Catechin	ND	ND	ND	+	ND	+
Chlorogenic acid	+	+	+	ND	+	+
Cinnamicbenzenepropenoic acid	ND	ND	ND	ND	ND	+
Coumaric acid	ND	+	ND	ND	ND	ND
Dimethoxy-quercetin	ND	ND	ND	+	ND	ND
Ellagic acid	ND	ND	ND	+	ND	+
Epigallocatechin gallate	+	ND	ND	ND	ND	ND
Ferulic acid	ND	+	ND	ND	ND	ND
Feruloyl-quinic acid	+	+	+	ND	+	+
Furosinin	ND	ND	+	ND	ND	ND
Gallic acid	ND	+	ND	+	ND	+
Hyperoside	+	+	+	ND	+	+
Isoquercitrin	+	+	+	ND	+	+
Isorhamnetin	ND	+	+	ND	ND	ND
Isorhamnetin-3-rutinoside-7-glucoside	ND	+	ND	ND	ND	ND

Phenolic compounds profile	Arrayán (<i>L. apiculata</i>)	Calafate (<i>B. microphylla</i>)	Chequén (<i>L. chequen</i>)	Maqui (<i>A. chilensis</i>)	Meli (<i>A. meli</i>)	Murtilla (<i>U. molinae</i>)
Isorhamnetin-3-galactoside	ND	+	ND	ND	ND	ND
Isorhamnetin-3-glucoside	ND	+	ND	ND	ND	ND
Isorhamnetin-3-rutinoside	ND	+	ND	ND	ND	ND
Isorhamnetin-3-(600-acetyl)- hexoside	ND	+	ND	ND	ND	ND
Isorhamnetin-3- malonylgalactoside	ND	+	ND	ND	ND	ND
Isorhamnetin-3- malonylglucoside	ND	+	ND	ND	ND	ND
Kaempferol	ND	+	ND	ND	ND	+
Kaempferol-deoxyhexoside	ND	+	ND	ND	ND	ND
Myricetin	+	+	+	+	+	+
Myricetin-3-rutinoside-7- glucoside	ND	+	ND	ND	ND	ND
Myricetin-3-glucoside	ND	+	ND	+	ND	ND
Myricetin-3-rutinoside	ND	+	ND	ND	ND	ND
Myricetin-3-O-rhamnose	+	ND	ND	ND	ND	ND
Myricetin-3-galactoside	ND	+	ND	ND	ND	ND
Neochlorogenic acid	+	+	+	ND	+	+
Protocatechuic	ND	ND	ND	+	ND	ND
Protocatechuic 3,4-Dihydroxybenzoic	ND	ND	ND	ND	ND	+
p-coumaric acid	ND	ND	ND	+	ND	+
Quercetin	+	+	+	+	+	+
Quercetin-3-rutinoside-7- glucoside	ND	+	ND	ND	ND	ND
Quercetin-3-galactoside	ND	+	ND	+	ND	ND
Quercetin-3-rutinoside	ND	+	ND	ND	ND	ND
Quercetin-3-glucoside	ND	+	ND	+	ND	ND
Quercetin-3- malonylgalactoside	ND	+	ND	ND	ND	ND
Quercetin-3-malonylglucoside	ND	+	ND	ND	ND	ND
Quercetin-3-rhamnoside	ND	+	ND	ND	ND	ND
Quercetin-galloyl-hexoside	ND	ND	ND	+	ND	ND
Quercetin-3-(600-acetyl)- hexoside 1	ND	+	ND	ND	ND	ND
Quercetin-3-(600-acetyl)- hexoside 2	ND	+	ND	ND	ND	ND

Phenolic compounds profile	Arrayán (<i>L. apiculata</i>)	Calafate (<i>B. microphylla</i>)	Chequén (<i>L. chequen</i>)	Maqui (<i>A. chilensis</i>)	Meli (<i>A. meli</i>)	Murtilla (<i>U. molinae</i>)
Quercetin-3-rhamnoside	ND	+	ND	ND	ND	ND
Quercetin-3-O-(6"-O-galloyl)-hexose	+	ND	ND	ND	ND	ND
Quercetin-3-O-glucose (isoquercitrin)	+	ND	ND	ND	ND	ND
Rutin	+	+	+	ND	+	+
Rutin hydrate	ND	ND	ND	+	ND	ND
Vanillic 4-Hydroxy-3-methoxybenzoic acid	ND	ND	ND	ND	ND	+
Unknown quinic acid derivative	+	ND	+	ND	ND	ND
Unknown gallotannin	ND	ND	+	ND	ND	ND
References	[8, 11, 14]	[14, 15, 48]	[8, 14]	[48, 81]	[14]	[14, 74, 79]

+, presence of compounds in fruits.
ND, not detected.

Table 2. Identification of phenolic compounds in native Chilean fruits.

Anthocyanin profile	Arrayán (<i>L. apiculata</i>)	Calafate (<i>B. microphylla</i>)	Chequén (<i>L. chequen</i>)	Maqui (<i>A. chilensis</i>)	Meli (<i>A. meli</i>)	Murtilla (<i>U. molinae</i>)
Delphinidin-3-glucoside	ND	+	ND	+	ND	+
Cyanidin-3-glucoside	ND	+	ND	+	ND	+
Petunidin-3-glucoside	ND	+	ND	ND	ND	ND
Peonidin-3-glucoside	ND	+	ND	ND	ND	+
Malvidin-3-glucoside	ND	+	ND	ND	ND	ND
Delphinidin-3-rutinoside	ND	+	ND	ND	ND	ND
Cyanidin-3-rutinoside	ND	+	ND	ND	ND	ND
Petunidin-3-rutinoside	ND	+	ND	ND	ND	ND
Peonidin-3-rutinoside	ND	+	ND	ND	ND	ND
Malvidin-3-rutinoside	ND	+	ND	ND	ND	ND

Anthocyanin profile	Arrayán (<i>L. apiculata</i>)	Calafate (<i>B. microphylla</i>)	Chequén (<i>L. chequen</i>)	Maqui (<i>A. chilensis</i>)	Meli (<i>A. meli</i>)	Murtilla (<i>U. molinae</i>)
Delphinidin-3-sambubioside	ND	ND	ND	+	ND	ND
Cyanidin-3-sambubioside	ND	ND	ND	+	ND	ND
Delphinidin-3-rutinoside-5-glucoside	ND	+	ND	ND	ND	ND
Petunidin-3-rutinoside-5-glucoside	ND	+	ND	ND	ND	ND
Malvidin-3-rutinoside-5-glucoside	ND	+	ND	ND	ND	ND
Delphinidin-3-sambubioside-5-glucoside	ND	ND	ND	+	ND	ND
Cyanidin-3-sambubioside-5-glucoside	ND	ND	ND	+	ND	ND
Delphinidin-3,5-dihexoside	ND	+	ND	ND	ND	ND
Cyanidin-3,5-dihexoside	ND	+	ND	ND	ND	ND
Petunidin-3,5-dihexoside	ND	+	ND	ND	ND	ND
Peonidin-3,5-dihexoside	ND	+	ND	ND	ND	ND
Malvidin-3,5-dihexoside	ND	+	ND	ND	ND	ND
Delphinidin-3,5-diglucoside	ND	ND	ND	+	ND	ND
Cyanidin-3,5-diglucoside	ND	ND	ND	+	ND	ND
Delphinidin-3-O-arabinoside	ND	+	ND	ND	ND	ND
Peonidin-3-O-arabinoside	ND	+	ND	ND	ND	+
Peonidin-3-O-di-hexoside	ND	+	ND	ND	ND	+
Cyanidin-3-O-di-hexoside	+	ND	ND	ND	ND	ND
Cyanidin-3-O-galactoside	ND	ND	+	ND	+	ND

Anthocyanin profile	Arrayán (<i>L. apiculata</i>)	Calafate (<i>B. microphylla</i>)	Chequén (<i>L. chequen</i>)	Maqui (<i>A. chilensis</i>)	Meli (<i>A. meli</i>)	Murtilla (<i>U. molinae</i>)
Petunidin-3-O-galactoside	+	+	+	ND	+	+
Malvidin-3-O-galactoside	+	ND	ND	ND	ND	ND
Delphinidin-3-O-glucoside	ND	+	ND	ND	ND	ND
Cyanidin-3-O-glucoside	+	ND	+	ND	+	ND
Petunidin-3-O-glucoside	+	ND	+	ND	+	+
Peonidin-3-O-glucoside	+	+	+	ND	ND	+
Malvidin-3-O-glucoside	+	+	+	ND	+	ND
Cyanidin-3-O-rutinoside	ND	ND	ND	ND	ND	+
Petunidin-3-O-rutinoside	ND	+	ND	ND	ND	+
Cyanidin-3-O-(6-succinoyl)-glucoside	ND	+	ND	ND	ND	+
Malvidin-3-O-(6-coumaroyl) glucoside	ND	+	ND	ND	ND	ND
Petunidin-3-O-(6-acetyl) glucoside	ND	+	ND	ND	ND	ND
Malvidin-3-O-(6-acetyl) galactoside	+	+	ND	ND	ND	ND
References	[7, 8, 10]	[7, 8, 10, 14, 48, 78]	[8, 10, 14]	[38, 46, 48, 75, 78, 80, 81]	[8, 14]	[10, 14, 48, 79]

+: presence of compounds in fruits.
ND, not detected.

Table 3. Identification of anthocyanins in native Chilean fruits.

Genotype, environmental factors, and geographical location are among the main causes for the differences in the antioxidant capacity in native Chilean fruits, since in all studies, fruits were collected in different locations. Mariangel et al. [15] analyzed Calafate fruit antioxidant capacity by DPPH method from different sites in southern Chile (Mañihuales and El Blanco; Aysén and Temuco and Lonquimay; Araucanía). They found that more southern provenances (Mañihuales and El Blanco) showed a higher antioxidant capacity—9.4 and 7.5 TE g⁻¹ of DW, respectively—than northernmost provenances (Temuco and Lonquimay) with 5.2 and 3.3 TE

g^{-1} DW, respectively. This suggests that growth conditions have a direct influence on the content of nutraceutical compounds in fruits, as total phenols in Calafate also showed the same trend: 16.1 mg gallic acid equivalent (GAE) g^{-1} DW (Lonquimay) and 34.6 mg GAE g^{-1} DW (Mañihuales). Thus, fruits from the southernmost region exhibited higher levels of total phenols.

Several types of phenolic compounds have been reported in native Chilean “superfruits,” including caffeic acid, ferulic acid, gallic acid, myricetin, *p*-coumaric acid, and others (**Tables 2 and 3**) [8, 14, 15, 47, 48, 74]. In native berries, total phenolics have been analyzed by Ruiz et al. [48] using the Folin-Ciocalteu method. The results showed a higher total phenol content for Maqui (97 μmol GAE g^{-1} FW) followed by Calafate (87 μmol GAE g^{-1} FW) and Murtilla (32 μmol GAE g^{-1} FW). However, no statistically significant differences were found between Maqui and Calafate. Afterward, Brito et al. [14] found higher values for Calafate (65 mg GAE g^{-1} DW) than for Arrayán (27 mg GAE g^{-1} DW), Meli (17 mg GAE g^{-1} DW), Murtilla (9 mg GAE g^{-1} DW), and Chequén (5 mg GAE g^{-1} DW). In addition, these studies have recognized anthocyanins as the most important compounds in native Chilean fruits (**Table 3**) [10, 14, 47, 48, 75–80].

Anthocyanins in Calafate fruits from the Aysén and Magallanes Regions, analyzed by HPLC-DAD, showed total anthocyanin concentrations between 14 and 26 μmol g^{-1} FW, corresponding to the highest values in fruits from the Aysén Region [48]. Comparable anthocyanin values as in Calafate were found in Maqui (16 and 20 μmol g^{-1} FW), whereas the lowest values were found in Murtilla (mean 0.2 μmol g^{-1} FW) and in Blueberry (2.0 μmol g^{-1} FW). The lowest results in Murtilla could be explained by the weaker coloration (rose) of their fruits compared with the black and blue-purple color of the other analyzed fruits [48]. In this context, Mariangel et al. [15] reported differences among Calafate fruits collected in different sites of the Araucanía (Temuco and Lonquimay) and Aysén Regions (Mañihuales and El Blanco). Higher values of cyanidin were found in El Blanco (0.6 mg g^{-1} DW), followed by Temuco (0.2 mg g^{-1} DW), Mañihuales (0.1 mg g^{-1} DW), and Lonquimay (0.06 mg g^{-1} DW). These results suggest that anthocyanin concentrations vary depending on the different agro-characteristics of the growth areas and the fruit-ripening time. Brito et al. [14] reported anthocyanin contents (in mg cyaniding 3-O-glucoside g^{-1} of DW) with higher values in Calafate fruits (51.6) than in Arrayán (15.2), Meli (13), Murtilla (6.85), and finally Chequén (1). Therefore, it is reported that there is higher anthocyanin content in fruits of Calafate and Maqui compared with other native berries [7, 14, 48, 81].

Due to the difficulty of having fresh fruits rich in antioxidants for consumption out of season, it is very important to know the effect of fruit preservation techniques on the content of bioactive compounds. Among the common techniques in use (convective hot-air, freeze drying, and direct cold), native Chilean fruits have demonstrated minor variation in the concentration of phenolic compounds and antioxidant activity compared with the fresh fruits [46, 82]. The effect of freeze-drying and direct cold on the content of bioactive compounds in native Chilean fruits are the least studied of these techniques, and therefore, they should be explored because cold storage in the postharvest period of these berries may produce fewer changes in the antioxidant levels.

3.2. Oxidative stress and antioxidant response in human pathophysiological disorders

Under normal conditions, the human body produces free radicals and other reactive oxygen species (ROS) [29, 83]. ROS are molecules characterized by an unpaired electron in an atomic orbital, being highly unstable, such as hydroxyl radical, superoxide anion radical, hydrogen peroxide, oxygen singlet, hypochlorite, nitric oxide radical, and peroxynitrite radical [83]. In the human body, the ROS molecules are produced in the mitochondria, peroxisomes, in inflammation, phagocytosis processes, and ischemia. They are exacerbated by exposure to stress conditions such as ozone, cigarette smoking, air pollutants, and industrial chemicals, among others [84–86]. The ROS have a high affinity for organic molecules (proteins, carbohydrates, and lipids), causing oxidative stress, damage in biomembranes, and altering body homeostasis [87]. The body counteracts the damage induced by ROS by activating antioxidant systems, which are stable molecules able to donate an electron to the free radical, neutralizing it and reducing ROS damage [88, 89]. The human metabolism produces enzymatic antioxidants such as superoxide dismutase, catalase, xanthine oxidase, lipogenase, and cyclooxygenase, and nonenzymatic compounds such as glutathione, ubiquinol, and uric acid [90]. However, it is also necessary to supply other antioxidants in the diet to strengthen the antioxidant capacity. Among them, vitamin E (α -tocopherol), vitamin C (ascorbic acid), and B-carotene are important. These antioxidants reduce the process of lipid peroxidation, preventing or decreasing oxidative reactions and cell damage [91, 92]. In tissues injured by infection, heat, hypertoxia trauma, and toxin-enhanced oxidative stress, processes are induced in the short-term [36]. To counteract the oxidative damage in tissues, transport of antioxidant enzymes (e.g., xanthine oxidase, lipogenase, and cyclooxygenase) and activation of phagocytes related to the release of free iron, copper ions, or a disruption of the electron transport chains of oxidative phosphorylation take place [36]. However, when the conditions of oxidative damage are higher than antioxidant defense responses, a critical imbalance between free radical generation and antioxidant defenses occurs. This imbalance in the human body induces complications such as diabetes mellitus, onset, promotion or progression of cancer, and neurodegenerative damage such as Parkinson's disease, among others [93–95]. Epidemiological evidence suggests that diets high in antioxidants reduce the incidence of heart disease, cancer, and neurological disorders, altering the inflammatory process common in these diseases [96–100]. Despite the wealth of information that relates to the consumption of fruits in general with the prevention of diseases linked to oxidative stress, studies into native Chilean fruits are limited.

3.3. Native Chilean fruits as a source of antioxidants

Antioxidant compounds in Chilean berries, such as phenolic acids, flavonoids, flavanols, anthocyanins, and procyanidins, among others, have been widely studied for their highly protective effect on human health, particularly with respect to age-related diseases and pathophysiological disorders related to oxidative stresses [6, 11, 37, 69, 82, 86, 101–104]. Antioxidants have an important role as anti-inflammatory or cancer chemopreventive compounds and against degenerative disorders, decreasing the risk of oxidative stress [6, 99, 105]. Furthermore, antho-

cyanins in berry fruits have a positive effect on human health, related to their capacity to act as antioxidants, and the protective effect in chronic diseases such as diabetes, cardiovascular diseases, and different type of cancers [6, 10, 14, 64, 106, 107]. Regarding the health beneficial properties of fruits, it is important to study different aspects: the species, the composition of bioactive compounds, their antioxidant capacity, and the capacity of different compounds to modulate the transcription factors of enzymes that induce inflammatory diseases [108, 109]. In this context, the traditional use of the plants is also important. Folk medicine in Chile has used leaves and fruits of Arrayán, Calafate, Chequén, Maqui, Meli, and Murtilla to treat throat pain, ulcers, inflammation, and kidney pain disorders [5, 41, 43]. Interestingly, the richness, abundance, and diversity of bioactive compounds in berries of the Chilean native species have shown effects against some pathophysiological disorders (inflammation, diabetes, and cardiovascular) as reported by Fredes et al. [69], Reyes-Farias et al. [6], Alonso [37], Wellen and Hotamisligil [101], Glass and Witztum [104], Lipfert et al. [86], Fuentes et al. [11], and Genskowsky et al. [82].

Inflammation is a defensive mechanism of the organism to specific noxa (factor producing damage), involving different cellular or humoral agents. Its purpose is to restore the body homeostasis, eliminating the noxae. When the inflammatory process becomes self-perpetuating, it ceases to be beneficial and becomes harmful [110–113]. Cell membrane damage activates the phospholipase A2, favoring the synthesis of arachidonic acid, which serves as a substrate for the formation of lipoxygenase and promotes the oxygenase cycle and leukotriene synthesis, which in turn induce the synthesis of prostaglandins and thromboxanes [114]. This promotes neutrophil chemotaxis, ultimately phagocytizing the damaged cell [115]. In addition, leukotriene favors vascular permeability, facilitating the influx of neutrophils to the injured tissue. In general, berries are important inhibitors of inflammatory processes due to the phenolic compounds like anthocyanins present in their fruits [116–121]. This has been supported by reports about moderate consumption of raspberry, strawberry, and bilberry (*Vaccinium myrtillus*) juices and green and black tea that can help prevent the development of early atherosclerosis [118]. Consumption of lingonberry (*Vaccinium vitis-idaea*) juice for 10 weeks has an anti-inflammatory effect on salt-induced hypertension in rat models, probably due to high polyphenol concentrations in the juice [119]. In wild blueberries, the fruits have provided *in vivo* evidence of the improvement or the prevention of metabolic disturbances associated with developing obesity, particularly a systemic low-grade inflammation and hypertension in mice [120]. In the case of strawberry, its tannins (as enriched extract or as pure compounds) are able to act on gastric epithelial cells, thereby inhibiting the inflammatory response [121]. More detailed information about the berries and their anti-inflammatory properties has been reported by Yang and Kortensniemi [122] and Joseph et al. [123]. Studies with native berries such as Maqui and Calafate fruits have given evidence that the compounds of these fruits can be considered a good anti-inflammatory agent [116, 124]. The anti-inflammatory activity has been shown *in vivo* in the ears of mice and *in vitro* using macrophages and guinea pigs [125–127]. Rouanet et al. [118] also showed that leaf extracts of these species have anti-inflammatory activity in mice, showing that leaf extracts containing quercetin and kaempferol can reduce inflammation.

Diabetes has been recognized as one of the most important chronic diseases in the world [128]. According to the International Diabetes Federation (IDF), 400 million people worldwide had diabetes in 2013, and it could reach 642 million by 2040 [128]. In 2013 alone, US\$548 billion was spent on diabetes management [128]. Therefore, it is a great challenge to find alternatives to reduce this global epidemic. Type II diabetes comprises disease groups of diverse etiology characterized by the presence of chronic hyperglycemia, altering the secretion and action of insulin, as well as alterations in the metabolism of carbohydrates, proteins, and lipids [128, 129]. Type II diabetes represents over 90% of diabetes cases, and its etiology involves both genetic and environmental factors [130]. In the last few years, a gradual increase in incidences has been reported, inducing metabolic alterations and cardiovascular complications [129–131]. Early treatment with dietary and/or pharmacological hygienic measures in patients with prediabetic states can reduce the incidence of diabetes [132]. However, clearly there is a genetic predisposition that is favored by some factors such as obesity or a sedentary lifestyle [133–135]. In this sense, the adipose tissue sets free inflammatory mediators such as interleukins, tumor necrosis factor (TNF- α), or free fatty acids, which increase insulin resistance and oxidative stress [130, 136, 137]. Most of the reports about this disease comprise the effects of commercial berries [138]. Thus, preclinical and clinical studies have suggested that consumption of commercial berries has health benefits with preventive effects on diabetes, improving insulin resistance [122, 139–142]. Studies in obesity-prone rats with a diet containing 2% (wt/wt) freeze-dried powder of highbush blueberry reduced the phenotypes of metabolic syndrome, affecting the gene transcripts of the peroxisome proliferator-activated receptors in adipose and muscle tissues involved in fat and glucose metabolism [143]. This may be due to fibers and/or polyphenols present in the berry fruits. Powder from lingonberries did not change the insulin curve in humans, when consumed together with added glucose [139]. Mursu et al. [140] reported that the intake of berries in the diet may reduce risk of type 2 diabetes in Finnish men. In addition, consumption of blackcurrant (*Ribes nigrum*) extract in amounts roughly equivalent to 100 g in fruit drinks with low sugar and administered immediately before a high-carbohydrate meal reduced postprandial glycemia, insulinemia, and incretin secretion, being beneficial to human health [141]. Further information about the link between berries and their anti-diabetic properties is available in Yang and Kortessniemi [122] and Tsuda [142]. Nevertheless, there are more limited reports in native Chilean fruits in the form of *in vitro* and *in vivo* studies. In this context, Dai and Mumper [65] reported that in *in vitro* studies, Maqui fruits have hypoglycemic effects that inhibit α -amylases and α -glucosidases, enzymes involved in the carbohydrate metabolism. In line with this evidence, the inhibition of both enzymes by Maqui fruits was also confirmed by Schreckinger et al. [144]. Using *in vivo* assays, Fredes et al. [78] reported the anti-diabetic properties of Maqui fruits in mice. They showed that oral administration of a standardized anthocyanin-rich formulation from Maqui fruits decreased blood glucose in obese hyperglycemic mice. It has been suggested that Maqui fruits could act by inhibiting sodium glucose cotransporter in the small intestine [145]. However, more studies are needed to confirm this physiological mechanism involved in reducing blood glucose. The results of *in vitro* studies of the biological effects of phenolic compounds are questioned due to the limited bioavailability and absorption of these compounds in the human body [146].

Cardiovascular diseases are a heterogeneous group of pathologies, the common substrate of which is the alteration of different arteries of the body regardless of caliber of arteries [147, 148]. In particular, these supply the brain, heart, lower limbs, and aorta [149]. The cascade of events for atherosclerosis are proliferation of smooth muscle cells, recruitment of inflammatory cells, and lipid deposits within the blood vessel walls, forming plaques of atheroma [149, 150]. This formation prevents normal tissue irrigation, inducing ischemia reduction or loss of blood flow in a tissue [150]. If the atheromatous plaque ruptures, the body in an attempt to repair activated coagulation cascade induces the formation of a platelet plug, which totally or partially obstructs the flow distally [151]. Therefore, the tissues supplied by the artery suffer hypoxia or anoxia due to the induction of tissue necrosis [149, 152, 153]. Plant antioxidants have been shown to reduce cellular oxidative damage and to protect against cardiovascular diseases [154]. Berry consumption has been known to benefit human health with preventive effects on cardiovascular diseases. Thus, Erlund et al. [155] reported that the consumption of moderate amounts of berries such as bilberries, nectar of lingonberries, blackcurrant, strawberry puree, cold-pressed chokeberry (*Aronia melanocarpa*), and raspberry juice resulted in favorable changes in platelet function, high density lipoprotein (HDL) cholesterol, and blood pressure in male and female volunteers, concluding that the berries may play a role in the prevention of cardiovascular disease. Afterward, Basu et al. [156] deepened the evidence about berry-rich diet that controls the risk of chronic diseases among them the cardiovascular risk. Interestingly, Oudot et al. [157] reported that a high salt diet (8% NaCl) with 2 g/day berries can prevent the cardiac alterations independently of changes in systolic pressure in rats. This was verified by Yang and Kortseniemi [122] and Huang et al. [158], who highlighted that berries are an essential fruit group in heart-healthy diets as a supplementary option to better prevent and control cardiovascular disease in humans. More details are available in Zhu et al. [159] and Rodriguez-Mateos et al. [160]. In the case of native Chilean fruits, the preclinical and clinical studies are more limited, although a recent interest in the study of these berries as a beneficial food to protect the heart is growing. Fredes et al. [69] found that Maqui fruits can significantly reduce the cardiac injury produced by ischemia-reperfusion (I/R) in rat heart *in vivo*. The I/R injury occurs after a myocardial ischemia, and it is known to generate free radicals, heart injury, and necrosis [69, 161, 162]. Therefore, the high level of phenolic compounds and antioxidant activity of this endemic berry can scavenge free radicals produced by I/R and protect the heart [69]. Similarly, concentrated Maqui juice has a high capacity for the oxidation of low-density lipoproteins, which is considered one of the first steps in the development of atherosclerosis [163]. In this sense, Fuentes et al. [11] suggested that Arrayán fruit extracts could protect endothelium-dependent vasodilation (measure to probe endothelial function in different pathophysiological disorders), which is impaired by high glucose [11]. Consequently, they consider that the extract may have an important use in the prevention of vascular damage induced by high glucose. In addition, Falkenberg et al. [164] showed an inhibition of “platelet aggregation” (induced by adenosine diphosphate and collagen) in sheep and human blood through the application of Arrayán and Chequén extracts, which was confirmed by the inhibition of platelet surface activation markers. Afterward, research showed that Murtilla fruits demonstrated vasodilator activity in the aortic rings [165]. Another important damage parameter used as a marker for the risk of developing heart disease is the

low-density lipoproteins (LDL). Maqui extracts may reduce oxidative modifications of LDL in overweight people and smokers [124].

Finally, all the properties mentioned of the native Chilean fruits place them in the category of “superfruits” due to their excellent biological effects on human health. Thus, these “superfruits” could be used as nutraceuticals and functional foods with potential use in the human health industry.

4. Conclusion

We conclude that Arrayán, Chequén, Maqui, Meli, and Murtilla fruits are rich in antioxidant compounds with high antioxidant power, such as anthocyanins. The results show that the consumption of native Chilean fruits reduces the risk of pathophysiological disorders such as inflammation, diabetes, and cardiovascular disease due to their bioactive compounds. Therefore, these berries have a potential for increased use in the functional food and nutraceutical industries.

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Author details

Elizabeth M. Ulloa-Inostroza¹, Eric G. Ulloa-Inostroza², Miren Alberdi^{1,3},
Daniela Peña-Sanhueza¹, Jorge González-Villagra¹, Laura Jaakola⁴ and
Marjorie Reyes-Díaz^{1,3*}

*Address all correspondence to: marjorie.reyes@ufrontera.cl

1 Center of Plant, Soil Interaction and Natural Resources Biotechnology, Scientific and Technological Bioresource Nucleus (BIOREN), Universidad de La Frontera, Temuco, Chile

2 Department of Internal Medicine, Faculty of Medicine, Universidad de La Frontera, Temuco, Chile

3 Department of Chemical Sciences and Natural Resources, Faculty of Engineering and Sciences, Universidad de La Frontera, Temuco, Chile

4 Department of Arctic and Marine Biology UiT, The Arctic University of Norway, Tromsø, Norway

References

- [1] Alvarado G, Moya JC. División Político-Administrativa y Censal 2007. Gobierno de Chile, Santiago-Chile. In: Instituto Nacional de Estadísticas, editors. 2008. 357 p.
- [2] Instituto Geográfico Militar. Ejército de Chile [Internet]. 2016. Available from: <https://www.igm.cl/div/MAPAIGM/CHILE%20COMPLETO/CHILE%20FISICO.jpg> [Accessed: 2026-08-23].
- [3] Niemeyer HM. Biologically active compounds from Chilean medicinal plants. In: Arnason JT, Matta R, Romeo JT, eds., Recent Advances in Phytochemistry. Phytochemistry of Medicinal Plants; Vol. 29, Plenum Press. New York, USA. 1995. 137–159 p. DOI: 10.1007/978-1-4899-1778-2_7.
- [4] Comisión Nacional del Medio Ambiente (CONAMA). Biodiversidad de Chile, Patrimonio y Desafíos. In: Ocho Libros Editores. Ed: Rovira J, Ugalde J, Stutzin M. Santiago, Chile. 2008.
- [5] Mølgaard P, Holler JG, Asar B, Liberna I, Rosenbæk LB, Jebjerg CP, Jørgensen L, Lauritzen J, Guzman A, Adersen A, Simonsen HT. Antimicrobial evaluation of Huilliche plant medicine used to treat wounds. J Ethnopharmacol. 2011;**138**:219–227. DOI: 10.1016/j.jep.2011.09.006.
- [6] Reyes-Farias M, Vasquez K, Ovalle-Marin A, Fuentes F, Parra C, Quiral V, Jimenez P, Garcia-Diaz DF. Chilean native fruit extracts inhibit inflammation linked to the pathogenic interaction between adipocytes and macrophages. J Med Food. 2015;**18**:601–608. DOI: 10.1089/jmf.2014.0031.
- [7] Ruiz A, Hermosín-Gutiérrez I, Vergara C, Von Baer D, Zapata M, Hitschfeld A, Obando L, Mardones C. Anthocyanin profiles in south Patagonian wild berries by HPLC-DAD-ESI-MS/MS. Food Res Int. 2013;**51**:706–713. DOI: 10.1016/j.foodres.2013.01.043.
- [8] Simirgiotis MJ, Bórquez J, Schmeda-Hirschmann G. Antioxidant capacity, polyphenol content and tandem HPLC-DAD-ESI/MS profiling of phenolic compounds from the South American berries *Luma apiculata* and *L. chequen*. Food Chem. 2013;**139**:289–299. DOI: 10.1016/j.foodchem.2013.01.089.
- [9] Retamales HA, Scharaschkin T. Comparative leaf anatomy and micromorphology of the Chilean myrtaceae: taxonomic and ecological implications. Flora Morphol Distribution Funct Ecol Plants. 2015;**217**:138–154. DOI: 10.1016/j.flora.2015.10.005.
- [10] Ramirez J, Zambrano R, Sepúlveda B, Kennelly EJ, Simirgiotis M. Anthocyanins and antioxidant capacities of six Chilean berries by HPLC–HR-ESI-ToF-MS. Food Chem. 2015;**176**:106–114. DOI: 10.1016/j.foodchem.2014.12.039.
- [11] Fuentes L, Valdenegro M, Gómez MG, Ayala-Raso A, Quiroga E, Martínez JP, Vinet R, Caballero E, Figueroa CR. Characterization of fruit development and potential health benefits of arrayan (*Luma apiculata*), a native berry of South America. Food Chem. 2016;**196**:1239–1247. DOI: 10.1016/j.foodchem.2015.10.003.

- [12] Landrum L. The myrtle family (Myrtaceae) in Chile. *Proc Calif Acad Sci USA*. 1988;**45**:277–317.
- [13] Murillo-Aldana J, Ruiz E. Revalidación de *Nothomyrcia* (Myrtaceae), un género endémico del Archipiélago de Juan Fernández. *Gayana Bot*. 2011;**682**:129–134. DOI: 10.4067/S0717-66432011000200002.
- [14] Brito A, Areche C, Sepúlveda B, Kennelly E, Simirgiotis M. Anthocyanin characterization, total phenolic quantification and antioxidant features of some Chilean edible berry extracts. *Molecules*. 2014;**19**:10936–10955. DOI: 10.3390/molecules190810936.
- [15] Mariangel E, Reyes-Díaz M, Lobos W, Bensch, E, Schalchli H, Ibarra P. The antioxidant properties of calafate (*Berberis microphylla*) fruits from four different locations in southern Chile. *Cienc Investig Agrar*. 2013;**40**:161–170. DOI: 10.4067/S0718-16202013000100014.
- [16] Chacón-Fuentes MA, Lizama MG, Parra LJ, Seguel IE, Quiroz AE. Insect diversity, community composition and damage index on wild and cultivated murtilla. *Cienc Investig Agrar*. 2016;**4**:57–67. DOI: 10.4067/S0718-16202016000100006.
- [17] Scalbert A, Manach C, Morand C, Remesy C. Dietary polyphenols and the prevention of diseases. *Crit Rev Food Sci Nutr*. 2005; **45**:287–306. DOI: 10.1080/1040869059096.
- [18] Lila MA, Ribnicky D, Rojo L, Rojas-Silva P, Oren A, Havenaar R, Janle E, Raskin I, Yousef G, Grace M. Complementary approaches to gauge the bioavailability and distribution of ingested berry polyphenolics. *J Agric Food Chem*. 2011;**60**:5763–5771. DOI: 10.1021/jf203526h.
- [19] Zaidi SM, Banu N. Antioxidant potential of vitamins A, E and C in modulating oxidative stress in rat brain. *Clin Chim Acta*. 2004;**340**:229–233. DOI: 10.1016/j.cccn.2003.11.003.
- [20] Zaidi SMKR, Al-Qirim TM, Banu N. Effects of antioxidant vitamins on glutathione depletion and lipid peroxidation induced by restraint stress in the rat liver. *Drugs R D*. 2005;**6**:157–165. DOI: 10.2165/00126839-200506030-00004.
- [21] Uttara B, Singh AV, Zamboni P, Mahajan R. Oxidative stress and neurodegenerative diseases: a review of upstream and downstream antioxidant therapeutic options. *Curr Neuropharmacol*. 2009;**7**:65–74. DOI: 10.2174/157015909787602823.
- [22] Sen GL. Remembering one's identity: the epigenetic basis of stem cell fate decisions. *FASEB J*. 2011;**25**:2123–2128. DOI: 10.1096/fj.11-182774.
- [23] Meerson FZ, Kagan VE, Kozlov YuP, Belkina LM, Arkhipenko YuV. The role of lipid peroxidation in pathogenesis of ischemic damage and the antioxidant protection of the heart. *Basic Res Cardiol*. 1982;**77**:465–485. DOI: 10.1007/BF01907940.
- [24] Valavanidis A, Vlachogianni T, Fiotakis K. Tobacco smoke: involvement of reactive oxygen species and stable free radicals in mechanisms of oxidative damage, carcinogenesis and synergistic effects with other respirable particles. *Int J Environ Res Publ Health*. 2009;**6**:445–462. DOI: 10.3390/ijerph6020445.

- [25] Khanna A, Guo M, Mehra M, Royal W. Inflammation and oxidative stress induced by cigarette smoke in Lewis rat brains. *J Neuroimmunol.* 2013;**254**:69–75. DOI: 10.1016/j.jneuroim.2012.09.006.
- [26] Adar SD, Klein R, Klein BE, Szpiro AA, Cotch MF, Wong TY, O'Neill MS, Shrager S, Barr RG, Siscovick DS, Kaufman JD. Air pollution and the microvasculature: a cross-sectional assessment of *in vivo* retinal images in the population-based multi-ethnic study of atherosclerosis (MESA). *PLoS Med.* 2010;**7**:1549–1277. DOI: 10.1371/journal.pmed.1000372.
- [27] Hiltermann JT, Lapperre TS, van Bree L, Steerenberg PA, Brahim JJ, Sont JK, Sterk PJ, Hiemstra PS, Stolk J. Ozone-induced inflammation assessed in sputum and bronchial lavage fluid from asthmatics: a new noninvasive tool in epidemiologic studies on air pollution and asthma. *Free Radic Biol Med.* 1999;**27**:1448–1454. DOI: 10.1016/S0891-5849(99)00191-4.
- [28] Fiedor J, Burda K. Potential role of carotenoids as antioxidants in human health and disease. *Nutrients.* 2014;**6**:466–488. DOI: 10.3390/nu6020466.
- [29] Bandyopadhyay U, Das D, Banerjee RK. Reactive oxygen species: oxidative damage and pathogenesis. *Curr Sci.* 1990;**77**:658–666.
- [30] Chang KC, Chung SY, Chong WS, Suh JS, Kim SH, Noh HK, Seong BW, Ko HJ, Chun KW. Possible superoxide radical-induced alteration of vascular reactivity in aortas from streptozotocin-treated rats. *J Pharmacol Exp Ther.* 1993;**266**:992–1000.
- [31] Hertog MGL, Kromhout D, Aravanis C, Blackburn H, Buz-ina R, Fidanza F, Iampoli S, Jansen A, Menotti A, Nedeljkovic S, Pekkarinen M, Simic BS, Oshima H, Feskens EJM, Hollman PCH, Katan MB. Flavonoid intake and long-term risk of coronary heart disease and cancer in the seven countries study. *Arch Intern Med.* 1995;**155**:281–286. DOI: 10.1001/archinte.1995.00430040053006.
- [32] Guerra-Araiza C, Álvarez-Mejía AL, Sánchez-Torres S, Farfan-García E, Mondragón-Lozano R, Pinto-Almazán R, Salgado-Ceballos H. Effect of natural exogenous antioxidants on aging and on neurodegenerative diseases. *Free Radic Res.* 2013;**47**:451–462. DOI: 10.3109/10715762.2013.795649.
- [33] Owen RW, Giacosa A, Hull WE, Haubner R, Spiegelhalter B, Bartsch H. The antioxidant/anticancer potential of phenolic compounds isolated from olive oil. *Eur J Cancer.* 2000;**36**:1235–1247. DOI: 10.1016/S0959-8049(00)00103-9.
- [34] Sala A, Recio MD, Giner RM, Manez S, Tournier H, Schinella G, Rios JL. Anti-inflammatory and antioxidant properties of *Helichrysum italicum*. *J Pharm Pharmacol.* 2002;**54**:365–371. DOI: 10.1211/0022357021778600.
- [35] Sun J, Chu YF, Wu XZ, Liu RH. Antioxidant and antiproliferative activities of common fruits. *J Agric Food Chem.* 2002;**50**:7449–7454. DOI: 10.1021/jf0207530.

- [36] Lobo V, Patil A, Phatak A, Chandra A. Free radicals, antioxidants and functional foods: impact on human health. *Pharmacogn Rev.* 2010;**4**:118–126. DOI: 10.4103/0973-7847.70902.
- [37] Alonso JR. Maqui (*Aristotelia chilensis*): un nutraceutico chileno de relevancia medicina. *Rev Farmacol Chile.* 2012;**5**:95–100.
- [38] Céspedes C, Valdez-Morales M, Avila J, El-Hafidi M, Alarcón J, Paredes-López O. Phytochemical profile and the antioxidant activity of Chilean wild black-berry fruits, *Aristotelia chilensis* (Mol.) Stuntz (Elaeocarpaceae). *Food Chem.* 2010a;**119**:886–895. DOI: 10.1016/j.foodchem.2009.07.045.
- [39] Hoffmann AE. Flora silvestre de Chile. 3rd ed. Ediciones Fundación Claudio Gay. Santiago, Chile. 1995.
- [40] Donoso C. Las especies arbóreas de los bosques templados de Chile y Argentina Autoecología. Ediciones Marisa Cuneo. Valdivia, Chile. 2006. 677 p.
- [41] Hoffmann A, Farga C, Lastra J, Veghazi E. Plantas Medicinales de Uso Común en Chile. Ediciones Fundación Claudio Gay. Santiago, Chile. 1992. 273 p.
- [42] Hoffman, A. Flora silvestre de Chile, zona araucana. 5 ed. Ediciones Fundación Claudio Gay. Santiago, Chile. 2005. 257 p.
- [43] Muñoz, O. Plantas medicinales de uso en Chile: química y farmacología. 2 ed. Ediciones Universitaria. Santiago, Chile. 2004.
- [44] Gironés-Vilaplana A, Mena P, García-Viguera C, Moreno D. A novel beverage rich in antioxidant phenolics: maqui berry (*Aristotelia chilensis*) and lemon juice. *LWT Food Sci Technol.* 2012;**47**:279–286. DOI: 10.1016/j.lwt.2012.01.020.
- [45] Araneda X, Quilamán E, Martínez M, Morales D. Elaboration and evaluation of maqui juice (*Aristotelia chilensis* (Mol.) Stuntz) by stream drag. *Sci Agropecu.* 2014;**5**:149–156. DOI: 10.17268/sci.agropecu.2014.03.05.
- [46] Brauch JE, Buchweitz M, Schweiggert RM, Carle R. Detailed analyses of fresh and dried maqui (*Aristotelia chilensis* (Mol.) Stuntz Berries and juice. *Food Chem.* 2016;**190**:308–316. DOI: 10.1016/j.foodchem.2015.05.097.
- [47] Ruiz A, Pastene E, Vergara C, Von Baer D, Avello M, Mardones C. Hydroxycinnamic acid derivatives and flavonol profiles of maqui (*Aristotelia chilensis*) fruits. *J Chil Chem Soc.* 2016;**61**:2792–2796. DOI: 10.4067/S0717-97072016000100010.
- [48] Ruiz A, Hermosín I, Mardones C, Vergara C, Herlitz C, Vega M, Dorau C, Winterhalter P, Von Baer D. Polyphenols and antioxidant activity of calafate (*Berberis microphylla*) fruits and other native berries from southern Chile. *J Agric Food Chem.* 2010;**58**:6081–6089. DOI: 10.1021/jf100173x.

- [49] Bottini CM, Bustos C, Bran D. Arbustos de la Patagonia, Calafates y Michay. Presencia. 1993;8:5–9.
- [50] Bottini MCJ, De Bustos A, Sanso AM, Jouve N, Poggio L. Relationships in Patagonian species of *Berberis* (Berberidaceae) based on the characterization of rDNA internal transcribed spacer sequences. Bot J Linnean Soc. 2007;153:321–328. DOI: 10.1111/j.1095-8339.2007.00586.x.
- [51] Fajardo Morales V. Estudio químico de las especies chilenas del género *Berberis*. Rev Latinoam Quim. 1987;18:46–50.
- [52] Landrum L. Revision of *Berberis* (Berberidaceae) in Chile and adjacent southern Argentina. Ann Missouri Bot Gard. 1999;86:793–834. DOI: <http://dx.doi.org/10.2307/2666170>.
- [53] Hoffman A. Flora Silvestre de Chile, Zona Araucana. 2ª ed. Ediciones Fundación Claudio Gay. Santiago, Chile. 1991. 285 p.
- [54] Gut B. Trees in Patagonia. In: Birkhäuser, editor. Eds.: Birkhäuser BioSciences. 2008. DOI: 10.1007/978-3-7643-8838-6.
- [55] Muñoz M, Barrera E, Meza I. El uso medicinal y alimenticio de plantas nativas y naturalizadas en Chile. In: Public. Ocac Museo Hist Nat de Chile. Santiago, Chile. 1981.
- [56] Massardo F, Rossi R. Valoración de la biodiversidad: usos medicinales de la flora native chilena. A y D. 1996;3:76–81.
- [57] Seguel I, Riveros M, Lehnebach C, Torres A. Antecedentes reproductivos y fenológicos de *Ugni molinae* Turcz. (Myrtaceae). Phytón. 1999;65:13–21.
- [58] Aguila Chacón C, Nahuelhual Muñoz L. Cultivo de murtilla (*Ugni molinae* turcz.) como alternativa de diversificación productiva para la agricultura familiar campesina de la cordillera de la costa. Agro Sur. 2008;36:158–167. DOI: 10.4206/agrosur.2008.v36n3-05.
- [59] Andrade N, Medel F, Montealegre J. Prospección del estado fitosanitario de arbustos frutales en la Región de los Lagos. Agro Sur. 1984;12:59–64.
- [60] Landrum L, Donoso C. *Ugni molinae* (Myrtaceae), a potential fruit crop for regions of Mediterranean, maritime and subtropical climates. Econ Bot. 1990;44:536–539.
- [61] Diaz Napal GN, Defago, M, Valladares G, Palacios S. Response of *Epilachna paenulata* to two flavonoids, Pinocembrin and quercetin, in a comparative study. J Chem Ecol. 2010;36:898–904. DOI: 10.1007/s10886-010-9823-1.
- [62] Ulloa-Inostroza EM, Alberdi M, Meriño-Gergichevich C, Reyes-Díaz M. Low doses of exogenous methyl jasmonate applied simultaneously with toxic aluminum improve the antioxidant performance of *Vaccinium corymbosum*. Plant Soil. DOI: 10.1007/s11104-016-2985-z.

- [63] Rice-Evans C, Miller NJ, Paganga G. Structure antioxidant activity relationships of flavonoids and phenolic acids. *Free Radic Biol Med.* 1996;**20**:933–956. DOI: 10.1016/0891-5849(95)02227-9.
- [64] Rice-Evans C, Miller N, Paganga G. Antioxidant properties of phenolic compounds. *Trends Plant Sci.* 1997;**2**:152–159. DOI: 10.1016/S1360-1385(97)01018-2.
- [65] Dai J, Mumper RJ. Plant phenolics: extraction, analysis and their antioxidant and anti-cancer properties. *Molecules.* 2010;**15**:7313–7352. DOI: 10.3390/molecules15107313.
- [66] Rubilar M, Jara C, Acevedo F, Gutierrez C, Sineiro J, Shene C. Extracts of maqui (*Aristotelia chilensis*) and Murta (*Ugni molinae* Turcz.): sources of antioxidant compounds and α -glucosidase/ α -amylase inhibitors. *J Agric Food Chem.* 2011;**59**:1630–1637. DOI: 10.1021/jf103461k.
- [67] Kedare S, Singh RP. Genesis and development of DPHH method of antioxidant assay. *J Food Sci Technol.* 2011;**48**:412–422. DOI: 10.1007/s13197-011-0251-1.
- [68] Brand-Williams W, Cuvelier ME, Berset C. Use of a free radical method to evaluate antioxidant activity. *LWT Food Sci Technol.* 1995;**28**:25–30. DOI: 10.1016/S0023-6438(95)80008-5.
- [69] Fredes C, Montenegro G, Zoffoli JP, Santander F, Robert P. Comparison of the total phenolic content, total anthocyanin content and antioxidant activity of polyphenol-rich fruits grown in Chile. *Cienc Investig Agrar.* 2014a;**41**:49–60. DOI: 10.4067/S0718-16202014000100005.
- [70] Céspedes C, El-Hafidi M, Pavon N, Alarcón J. Antioxidant and cardioprotective activities of phenolic extracts from fruits of Chilean blackberry *Aristotelia chilensis* (Elaeocarpaceae), maqui. *Food Chem.* 2008;**107**:820–829. DOI:10.1016/j.foodchem.2007.08.092.
- [71] Fredes C, Yousef G, Robert P, Grace M, Lila M, Gomez M, Gebauer M, Montenegro G. Anthocyanin profiling of wild maqui berries (*Aristotelia chilensis* (Mol.) Stuntz) from different geographical regions in Chile. *J Sci Food Agric.* 2014b;**94**:2639–2648. DOI: 10.1002/jsfa.6602.
- [72] Dávalos A, Gómez-Cordovés C, Bartolomé B. Extending applicability of the oxygen radical absorbance capacity (ORAC—fluorescein) assay. *J Agric Food Chem.* 2004;**52**:48–54. DOI: 10.1021/jf0305231.
- [73] Prior RL, Wu XL, Schaich K. Standardized methods for the determination of antioxidant capacity and phenolics in foods and dietary supplements. *J Agric Food Chem.* 2005;**53**:4290–4302. DOI: 10.1021/jf0502698.
- [74] Speisky H, López Alarcón C, Gómez M, Fuentes J, Sandoval Acuña C. First web-based database on total phenolics and oxygen radical absorbance capacity (ORAC) of fruits produced and consumed within the South Andes Region of South America. *J Agric Food Chem.* 2012;**60**:8851–8859. DOI: 10.1021/jf205167k.

- [75] Rodríguez K, Ah-Hen K, Vega-Gálvez A, López J, Quispe-Fuentes I, Lemus-Mondaca R, Gálvez-Ranilla L. Changes in bioactive compounds and antioxidant activity during convective drying of murta (*Ugni molinae* T.) berries. *Int J Food Sci Technol*. 2013;**49**:1–13. DOI: 10.1111/ijfs.12392.
- [76] Escribano-Bailón M, Alcalde-Eon C, Muñoz O, Rivas-Gonzalo J, Santos-Buelga C. Anthocyanins in berries of maqui (*Aristotelia chilensis* (Mol.) Stuntz). *Phytochem Anal*. 2006;**17**:8–14. DOI: 10.1002/pca.872.
- [77] Guerrero J, Ciampi L, Castilla A, Medel F, Schalchli H, Hormazabal E, Bensch E, Alberdi M. Antioxidant capacity, anthocyanins and total phenols of wild and cultivated berries in Chile. *Chil J Agric Res*. 2010;**70**:537–544. DOI: 10.4067/S0718-58392010000400002.
- [78] Fredes C, Montenegro G, Zoffoli JP, Gomez M, Robert P. Polyphenol content and antioxidant activity of maqui (*Aristotelia chilensis* (Molina) Stuntz) during fruit development and maturation in central Chile. *Chil J Agric Res*. 2012;**72**:582–589. DOI: 10.4067/S0718-58392012000400019.
- [79] Rojo LE, Ribnicky D, Logendra S, Poulev A, Rojas-Silva P, Kuhn P, Dorn R, Grace M, Lila MA, Raskin I. *In vitro* and *in vivo* anti-diabetic effects of anthocyanins from Maqui berry (*Aristotelia chilensis*). *Food Chem*. 2012;**131**:387–396. DOI: 10.1016/j.foodchem.2011.08.066.
- [80] Alfaro S, Mutis A, Quiroz A, Seguel I, Scheuermann E. Effects of drying techniques on murtilla fruit polyphenols and antioxidant activity. *J Food Res*. 2014;**5**:73–82. DOI: 10.5539/jfr.v3n5p73.
- [81] Tanaka J, Kadekaru T, Ogawa K, Hitoie S, Shimoda H, Hara H. Maqui berry (*Aristotelia chilensis*) and the constituent delphinidin glycoside inhibit photoreceptor cell death induced by visible light. *Food Chem*. 2013;**19**:129–137. DOI: 10.1016/j.foodchem.2013.01.036.
- [82] Genskowsky E, Puente LA, Pérez-Álvarez JA, Fernández-López J, Muñoz LA, Viuda-Martos M. Determination of polyphenolic profile, antioxidant activity and antibacterial properties of maqui [*Aristotelia chilensis* (Molina) Stuntz] a Chilean blackberry. *J Sci Food Agric*. 2016;**96**:4235–4242. DOI 10.1002/jsfa.7628.
- [83] Rodríguez K, Ah-Henb KS, Vega-Gálvez A, Vásquez V, Quispe-Fuentes I, Pilar Rojas P, Lemus-Mondaca R. Changes in bioactive components and antioxidant capacity of maqui, *Aristotelia chilensis* [Mol] Stuntz, berries during drying. *LWT Food Sci Technol*. 2016;**65**:537–542. DOI: 10.1016/j.lwt.2015.08.050.
- [84] Ohshima H, Tazawa H, Sylla BS, Sawa T. Prevention of human cancer by modulation of chronic inflammatory processes. *Mutat Res Fundam Mol Mech Mutagen*. 2005;**591**:110–122. DOI: 10.1016/j.mrfmmm.2005.03.030.
- [85] Joffe M. Infertility and environmental pollutants. *Br Med Bull*. 2003;**68**:47–70. DOI: 10.1093/bmb/ldg025.

- [86] Lipfert FW, Zhang J, Wyzga RE. Infant mortality and air pollution: a comprehensive analysis of US data for 1990. *J Air Waste Manag Assoc.* 2000;**50**:1350–1366. DOI: 10.1080/10473289.2000.10464168.
- [87] Vergara D, Ávila D, Escobar E, Carrasco-Pozo C, Sánchez A, Gotteland M. The intake of maqui (*Aristotelia chilensis*) berry extract normalizes H₂O₂ and IL-6 concentrations in exhaled breath condensate from healthy smokers—an explorative study. *Nutr J.* 2015. DOI: 10.1186/s12937-015-0008-1.
- [88] D'Autréaux B, Toledano MB. ROS as signalling molecules: mechanisms that generate specificity in ROS homeostasis. 2007;**8**:813–824. DOI: 10.1038/nrm2256.
- [89] Valko M, Leibfritz D, Moncol J, Cronin MTD, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. *Int J Biochem Cell B.* 2007;**39**:44–84. DOI: 10.1016/j.biocel.2006.07.001.
- [90] Cotelle N, Bernier JL, Catteau JP, Pommery J, Wallet JC, Gaydou EM. Antioxidant properties of hydroxyflavones. *Free Radic Biol Med.* 1996;**20**:35–43. DOI: 10.1016/0891-5849(95)02014-4.
- [91] Neergheen VS, Bahorun T, Taylor EW, Jen LS, Aruoma OI. Targeting specific cell signaling transduction pathways by dietary and medicinal phytochemicals in cancer chemoprevention. *Toxicology.* 2010;**278**:229–241. DOI: 10.1016/j.tox.2009.10.010.
- [92] Niki E, Noguchi N, Tsuchihashi H, and Gotoh N. Interaction among vitamin C, vitamin E, and beta-carotene. *Am J Clin Nutr.* 1995;**62**:1322–1326.
- [93] Zhang Y, Dawson VL, Dawson TM. Oxidative stress and genetics in the pathogenesis of Parkinson's disease. *Neurobiol Dis.* 2000;**7**:240–250. DOI: 10.1006/nbdi.2000.0319.
- [94] Dröge W. Free radicals in the physiological control of cell function. *Physiol Rev.* 2002;**82**:47–95. DOI: 10.1152/physrev.00018.2001.
- [95] Atack JM, Kelly DJ. Oxidative stress in campylobacter jejuni: responses, resistance and regulation. *Future Microbiol.* 2009;**4**:677–690. DOI: 10.2217/fmb.09.44.
- [96] Iborra M, Moret I, Rausell F, Bastida G, Aguas M, Cerrillo E, Nos P, Beltran B. Role of oxidative stress and antioxidant enzymes in Crohn's disease. *Biochem Soc Trans.* 2011;**39**:1102–1106. DOI: 10.1042/BST0391102.
- [97] Lin Y, Berg AH, Iyengar P, Lam TK, Giacca A, Combs TP, Rajala MW, Du X, Rollman B, Li W, Hawkins M, Barzilai N, Rhodes CJ, Fantus IG, Brownlee M, Scherer PE. The hyperglycemia-induced inflammatory response in adipocytes: the role of reactive oxygen species. *J Biol Chem.* 2005;**280**:4617–4626. DOI: 10.1074/jbc.M411863200.
- [98] Furukawa S, Fujita T, Shimabukuro M, Iwaki M, Yamada Y, Nakajima Y, Nakayama O, Makishima M, Matsuda M, Shimomura I. Increased oxidative stress in obesity and its impact on metabolic syndrome. *J Clin Invest.* 2004;**114**:1752–1761. DOI: 10.1172/JCI21625.
- [99] Urakawa H, Katsuki A, Sumida Y, Gabazza EC, Murashima S, Morioka K, Maruyama N, Kitagawa N, Tanaka T, Hori Y, Nakatani K, Yano Y, Adachi Y. Oxidative stress is associated with adiposity and insulin resistance in men. *J Clin Endocrinol Metab.* 2003;**88**:4673–4676. DOI: 10.1210/jc.2003-030202.

- [100] Ferrari N, Tosetti F, De Flora S, Donatelli F, Sogno I, Noonan DM, Albini A. Diet-derived phytochemicals: from cancer chemoprevention to cardio-oncological prevention. *Curr Drug Targets*. 2011;**13**:1909–1924. DOI: 10.2174/138945011798184227.
- [101] Wellen KE, Hotamisligil GS. Inflammation, stress, and diabetes. *J Clin Invest*. 2005;**115**:1111–1119. DOI: 10.1172/JCI200525102DS1.
- [102] Peña J. *Aristotelia chilensis*: a possible nutraceutical or functional food. *Med Chem*. 2015;**5**:378–382. DOI: 10.4172/2161-0444.1000289.
- [103] Stocker, R. Dietary and pharmacological antioxidants in atherosclerosis. *Curr Opin Lipidol*. 1999;**10**:589–597.
- [104] Glass CK, Witztum JL. Atherosclerosis. The road ahead. *Cell*. 2001;**104**:503–516. DOI: 10.1016/S0092-8674(01)00238-0.
- [105] Watson RR, Schönlaue F. Nutraceutical and antioxidant effects of a delphinidin-rich maqui berry extract Delphinol®: a review. *Minerva Cardioangiol*. 2015;**63**:1–12.
- [106] Priyadarsini RV, Nagini S. Cancer chemoprevention by dietary phytochemicals: promises and pitfalls. *Curr Pharm Biotechnol*. 2012;**13**:125–136. DOI: 10.2174/138920112798868610.
- [107] Zamora-Ros R, Fedirko V, Trichopoulou A, González CA, Bamia C, Trepo E, Nöthlings U, Duarte-Salles T, Serafini M, Bredsdorff L, Overvad K, Tjønneland A, Halkjaer J, Fagherazzi G, Perquier F, Boutron-Ruault MC, Katzke V, Lukanova A, Floegel A, Boeing H, Lagiou P, Trichopoulos D, Saieva C, Agnoli C, Mattiello A, Tumino R, Sacerdote C, Bueno-de-Mesquita HB, Peeters PH, Weiderpass E, Engeset D, Skeie G, Argüelles MV, Molina-Montes E, Dorronsoro M, Tormo MJ, Ardanaz E, Ericson U, Sonestedt E, Sund M, Landberg R, Khaw KT, Wareham NJ, Crowe FL, Riboli E, Jenab M. Dietary flavonoid, lignan and antioxidant capacity and risk of hepatocellular carcinoma in the European prospective investigation into cancer and nutrition study. *Int J Cancer*. 2013;**133**:2429–2443. DOI: 10.1002/ijc.28257.
- [108] Pojer E, Mattivi F, Jhonson D, Stokey C. The case for anthocyanin consumption to promote human health: a review. *Compr Rev Food Sci Food Saf*. 2013;**12**:483–508. DOI: 10.1111/1541-4337.12024.
- [109] Kang JH, Pasquale LR, Willett W, Rosner B, Egan KM, Faberowski N, Hankinson SE. Antioxidant intake and primary open-angle glaucoma: a prospective study. *Am J Epidemiol*. 2003;**158**:337–346. DOI:10.1093/aje/kwg167.
- [110] Zhang K, Zuo Y. GC-MS determination of flavonoids and phenolic and benzoic acids in human plasma after consumption of cranberry juice. *J Agric Food Chem*. 2004;**52**:222–227. DOI: 10.1021/jf035073r.
- [111] Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow?. *Lancet*. 2001;**357**:539–545. DOI: 10.1016/S0140-6736(00)04046-0.
- [112] Palapattu GS, Sutcliffe S, Bastian PJ, Platz EA, De Marzo AM, Isaacs WB, Nelson WG. Prostate carcinogenesis and inflammation: emerging insights. *Carcinogenesis*. 2005;**26**:1170–1181. DOI: 10.1093/carcin/bgh317.

- [113] Schwartsburd PM. Chronic inflammation as inductor of procancer microenvironment: pathogenesis of dysregulated feedback control. *Cancer Metastasis Rev.* 2003;**22**:95–102. DOI: 10.1023/A:1022220219975.
- [114] Szafran B, Borazjani A, Lee JH, Ross MK, Kaplan BLF. Lipopolysaccharide suppresses carboxylesterase 2 g activity and 2-arachidonoylglycerol hydrolysis: a possible mechanism to regulate inflammation. *Prostaglandins Other Lipid Mediat.* 2015;**121**:199–206. DOI: 10.1016/j.prostaglandins.2015.09.005.
- [115] Simmons DL, Botting RM, Ha T. Cyclooxygenase isozymes: the biology of prostaglandin synthesis and inhibition. *Pharmacol Rev.* 2004;**56**:387–437. DOI: 10.1124/pr.56.3.3.
- [116] Jiang M, Klein M, Zanger UM, Mohammad MK, Cave MC, Gaikwad NW, Dias NJ, Selcer KW, Guo Y, He J, Zhang X, Shen Q, Qin W, Li J, Li S, Xie W. Inflammatory regulation of steroid sulfatase: a novel mechanism to control estrogen homeostasis and inflammation in chronic liver disease. *J Hepatol.* 2016;**64**:44–52. DOI: 10.1016/j.jhep.2015.07.022.
- [117] Romanucci V, D'Alonzo D, Guaragna A, Di Marino C, Davinelli S, Scapagnini G, Di Fabio G, Zarrelli A. Bioactive compounds of *Aristotelia chilensis* Stuntz and their pharmacological effects. *Curr Pharm Biotechnol.* 2016;**17**:1:11.
- [118] Rouanet JM, Décordé K, Del Rio D, Auger C, Borges G, Cristol JP, Lean MEJ, Crozier A. Berry juices, teas, antioxidants and the prevention of atherosclerosis in hamsters. *Food Chem.* 2010;**118**:266–271. DOI: 10.1016/j.foodchem.2009.04.116.
- [119] Kivimäki AS, Siltari A, Ehlers PI, Korpela R, Vapaatalo H. Lingonberry juice negates the effects of a high salt diet on vascular function and low-grade inflammation. *J Funct Foods.* 2014;**7**:238–245.
- [120] Mykkänen OT, Huotari A, Herzig KH, Dunlop TW, Mykkänen H, Kirjavainen PV. Wild blueberries (*Vaccinium myrtillus*) alleviate inflammation and hypertension associated with developing obesity in mice fed with a high-fat diet. *PLoS One.* 2014. DOI: 10.1371/journal.pone.0114790.
- [121] Fumagalli M, Sangiovanni E, Vrhovsek U, Piazza S, Colombo E, Gasperotti M, Mattivi F, De Fabiani E, Dell'Agli M. Strawberry tannins inhibit IL-8 secretion in a cell model of gastric inflammation. *Pharmacol Res.* 2016;**111**:703–712. DOI: 10.1016/j.phrs.2016.07.028.
- [122] Yang B, Kortessniemi M. Clinical evidence on potential health benefits of berries. *Curr Opin Food Sci.* 2015;**2**:36–42. DOI: 10.1016/j.cofs.2015.01.002.
- [123] Joseph SV, Edirisinghe I, Burton-Freeman BM. Berries: anti-inflammatory effects in humans. *J Agric Food Chem.* 2014;**62**:3886–3903. DOI: 10.1021/jf4044056.
- [124] Davinelli S, Bertoglio JC, Zarrelli A, Pina R, Scapagnini G. A randomized clinical trial evaluating the efficacy of an anthocyanin-maqui berry extract (Delphinol®) on oxidative stress biomarkers. *J Anim Physiol Anim Nutr.* 2015;**34**:28–33. DOI: 10.1080/07315724.2015.1080108.

- [125] Céspedes C, Alarcon J, Avila J, Nieto A. Anti-inflammatory activity of *Aristotelia chilensis* Mol. (Stuntz) (Elaeocarpaceae). BLACPM. 2010b;9:91–99.
- [126] Schreckinger M, Wang J, Yousef G, Lila M, Gonzalez de Mejia E. Antioxidant capacity and *in vitro* inhibition of adipogenesis and inflammation by phenolic extracts of *Vaccinium floribundum* and *Aristotelia chilensis*. J Agric Food Chem. 2010;58:8966–8976. DOI: 10.1021/jf100975m.
- [127] Muñoz O, Christen P, Cretton S, Backhouse N, Torres V, Correa O, Costa E, Miranda H, Delporte C. Chemical study and anti-inflammatory, analgesic and antioxidant activities of the leaves of *Aristotelia chilensis* (Mol.) Stuntz. Elaeocarpaceae. 2011;63:849–859. DOI: 10.1111/j.2042-7158.2011.01280.x.
- [128] The IDF Diabetes Atlas Seventh Edition [Internet]. 2015. Organización Mundial de la Salud. 2016. Informe mundial sobre la diabetes. Available from: <http://www.idf.org/diabetesatlas>. [Accessed: 2016-01-18].
- [129] Muniyappa R, Montagnani M, Koh KK, Quon MJ. Cardiovascular actions of insulin. Endocr Rev. 2007;28:463–491. DOI: 10.1210/er.2007-0006.
- [130] Murdock KW, LeRoy AS, Lacourt TA, Duke DC, Heijnen CJ, Fagunde CP. Executive functioning and diabetes: the role of anxious arousal and inflammation. Psycho Neuro Endocrinol. 2016;71:102–109. DOI: 10.1016/j.psyneuen.2016.05.006.
- [131] Bacha F, Gidding SS, Pyle L, Katz LL, Kriska A, Nadeau KJ, Lima JAC, On behalf of the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) Study Group. Relationship of cardiac structure and function to cardiorespiratory fitness and lean body mass in adolescents and young adults with type 2 diabetes. J Pediatr. 2016. DOI: 10.1016/j.jpeds.2016.06.048.
- [132] Wild SH, Morling JR, McAllister DA, Kerssens J, Fischbacher C, Parkes J, Roderick PJ, Sattar N, Christopher D. Byrne CD, On behalf of the Scottish and Southampton Diabetes and Liver Disease Group, and the Scottish Diabetes Research Network Epidemiology Group. Type 2 diabetes and risk of hospital admission or death for chronic liver diseases. J Hepatol. 2016;64:1358–1364. DOI: 10.1016/j.jhep.2016.01.014.
- [133] Diouf I, Magliano DJ, Carrington MJ, Stewart S, Shaw JE. Prevalence, incidence, risk factors and treatment of atrial fibrillation in Australia: the Australian diabetes, obesity and lifestyle (AusDiab) longitudinal, population cohort study. Int J Cardiol. 2016;205:127–132. DOI: 10.1016/j.ijcard.2015.12.013.
- [134] Fukushima A, Lopaschuk GD. Cardiac fatty acid oxidation in heart failure associated with obesity and diabetes. Biochim Biophys Acta. 2016;1861:1525–1534. DOI: 10.1016/j.bbalip.2016.03.020.
- [135] Merger SR, Kerner W, Stadler M, Zeyfang A, Jehle P, Müller-Korbsch M, Holl RW, For the DPV Initiative, and the German BMBF Competence Network Diabetes mellitus. Prevalence and comorbidities of double diabetes. Diabetes Res Clin Pract. 2016;119:48–56. DOI: 10.1016/j.diabres.2016.06.003.

- [136] Orio F, Muscogiuri G, Nese C, Palomba S, Savastano S, Tafuri D, Colarieti G, La Sala G, Colao A, Yildiz BO. Obesity, type 2 diabetes mellitus and cardiovascular disease risk: an up to date in the management of polycystic ovary syndrome. *Eur J Obstet Gynecol Reprod Biol*. DOI: 10.1016/j.ejogrb.2016.08.026.
- [137] Zlobine I, Gopal K, Ussher JR. Lipotoxicity in obesity and diabetes related cardiac dysfunction. *Biochim Biophys Acta*. 2016;**1861**:1555–1568. DOI: 10.1016/j.bbalip.2016.02.011.
- [138] Huntley AL. The health benefits of berry flavonoids for menopausal women: cardiovascular disease, cancer and cognition. *Maturitas*. 2009;**63**:297–301. DOI: 10.1016/j.maturitas.2009.05.005.
- [139] Linderborg KM, Järvinen R, Lehtonen HM, Viitanen M, Kallio HPT. The fiber and/or polyphenols present in lingonberries null the glycemic effect of the sugars present in the berries when consumed together with added glucose in healthy human volunteers. *Nutr Res*. 2012;**32**:471–478. DOI: 10.1016/j.nutres.2012.06.004.
- [140] Mursu J, Virtanen JK, Tuomainen TP, Nurmi T, Voutilainen S. Intake of fruit, berries, and vegetables and risk of type 2 diabetes in Finnish men: the Kuopio Ischaemic heart disease risk factor study. *Am J Clin Nutr*. 2013. DOI: 10.3945/ajcn.113.069641.
- [141] Castro Acosta ML, Smith L, Miller RJ, McCarthy DI, Farrimond JA, Hall WL. Drinks containing anthocyanin-rich blackcurrant extract decrease postprandial blood glucose, insulin and incretin concentrations. *J Nutr Biochem*. 2016. DOI: 10.1016/j.jnutbio.2016.09.002.
- [142] Tsuda T. Recent progress in anti-obesity and anti-diabetes effect of berries. *Antioxidants*. 2016. DOI:10.3390/antiox5020013.
- [143] Seymour EM, Tanone II, Urcuyo-Llanes DE, Lewis SK, Kirakosyan A, Kondoleon MG, Kaufman PB, Bolling SF. Blueberry intake alters skeletal muscle and adipose tissue peroxisome proliferator-activated receptor activity and reduces insulin resistance in obese rats. *J Med Food*. 2011;**14**:1511–1518. DOI: 10.1089/jmf.2010.0292.
- [144] Schreckinger M, Lila M, Yousef G, Mejia E. Inhibition of glucosidase and amylase by *Vaccinium floribundum* and *Aristotelia chilensis* proanthocyanidins. In: Tunick and Gonzalez de Mejia; *Hispanic Foods: Chemistry and Bioactive Compounds ACS Symposium Series*; American Chemical Society. Washington, DC. 2012. 71–82 p. DOI: 10.1021/bk-2012-1109.ch006.
- [145] Hidalgo J, Flores C, Hidalgo MA, Perez M, Yañez A, Quiñones L, Caceres DD, Burgos RA. Delphinol standardized maqui berry extract reduces postprandial blood glucose increase in individuals with impaired glucose regulation by novel mechanism of sodium glucose cotransporter inhibition. *Panminerva Med*. 2014;**56**:1–7.
- [146] Crozier A, Jaganath IB, Clifford MN. Dietary phenolics: chemistry, bioavailability and effects on health. *Nat Prod Rep*. 2009;**26**:1001–1043. DOI: 10.1039/b802662a.
- [147] Moreno PR, Purushothaman KR, Sirol M, Levy P, Fuster V. Neovascularization in human atherosclerosis. *Circulation*. 2006;**113**:2245–2252. DOI: 10.1161/CIRCULATIONAHA.105.578955.

- [148] Lavie CJ, De Schutter A, Parto P, Jahangir E, Kokkinos P, Ortégac FB, Arena B, Milani RV. Obesity and prevalence of cardiovascular diseases and prognosis—the obesity paradox updated. *Prog Cardiovasc Dis*. 2016;**58**:537–547. DOI: 10.1016/j.pcad.2016.01.008.
- [149] Cuende JI, Pérez de Diego IJ, Godoy D. Enfermedades cardiovasculares y enfermedades inflamatorias sistémicas. *Clin Investig Arterioscler*. 2016;**28**:94–101. DOI: 10.1016/j.arteri.2015.07.001.
- [150] Kurata M, Nose M, Shimazu Y, Aoba T, Kohada Y, Yorioka S, Suehiro S, Fukuoka E, Matsumoto S, Watanabe H, Kumon Y, Okura T, Higaki J, Masumoto J. Microvasculature of carotid atheromatous plaques: hemorrhagic plaques have dense microvessels with fenestrations to the arterial lumen. *J Stroke Cerebrovasc Dis*. 2014;**23**:1440–1446. DOI: 10.1016/j.jstrokecerebrovasdis.2013.12.003.
- [151] Ross R. The pathogenesis of atherosclerosis: an update. *N Engl J Med*. 1986;**314**:488–500. DOI: 10.1056/NEJM198602203140806.
- [152] Barger AC, Beeuwkes R 3rd, Lainey LL, Silverman KJ. Hypothesis: *vasa vasorum* and neovascularization of human coronary arteries. A possible role in the pathophysiology of atherosclerosis. *N Engl J Med*. 1984;**310**:175–177. DOI: 10.1056/NEJM198401193100307.
- [153] Kordalewska M, Markuszewski MJ. Metabolomics in cardiovascular diseases. *J Pharm Biomed Anal*. 2015;**113**:121–136. DOI: 10.1016/j.jpba.2015.04.021.
- [154] World Health Organization [Internet]. 2012. World Health Organization. Global Atlas on Cardiovascular Disease Prevention and Control. (2012) Available from: http://www.who.int/cardiovascular_diseases/en/ [Accessed: 2012-02-16].
- [155] Erlund I, Koli R, Alfthan G, Marniemi J, Puukka P, Mustonen P, Mattila P, Jula A. Favorable effects of berry consumption on platelet function, blood pressure, and HDL cholesterol. *Am J Clin Nutr*. 2008;**87**:323–331.
- [156] Basu A, Rhone M, Lyons TL. Berries: emerging impact on cardiovascular health. *Nutr Rev*. 2010;**68**:168–177. DOI:10.1111/j.1753-4887.2010.00273.x.
- [157] Oudot C, Gomes A, Wang Z, Mateo P, Fischmeister R, Vieira H, Santos C, Brenner C. Beneficial effects of berries intake on survival and cardio-renal changes induced by high salt diet in Dahl/SS rat. Topic 27 – Hypertension, remodeling, arterial stiffness – B. *Arch Cardiovasc Dis Suppl*. 2015;**7**:185–186.
- [158] Huang H, Chen G, Liao D, Zhu Y, Xue X. Effects of berries consumption on cardiovascular risk factors: a meta-analysis with trial sequential analysis of randomized controlled trials. *Sci Rep*. DOI: 10.1038/srep23625.
- [159] Zhu Y, Miao Y, Meng Z, Zhong Y. Effects of vaccinium berries on serum lipids: a meta-analysis of randomized controlled trials. *Evid Based Complement Altern Med*. 2015. DOI: 10.1155/2015/790329.
- [160] Rodriguez-Mateos A, Heiss C, Borges G, Crozier A. Berry (poly)phenols and cardiovascular health. *J Agric Food Chem*. 2014;**62**:3842–3851. DOI: 10.1021/jf403757g.

- [161] Maxwell S, Lip G. Reperfusion injury: a review of the pathophysiology, clinical manifestations and therapeutic options. *Int J Cardiol.* 1997;**58**:95–117. DOI: 10.1016/S0167-5273(96)02854-9.
- [162] Dhalla NS, Elmoselhi AB, Hata T, Makino N. Status of myocardial antioxidants in ischemia–reperfusion injury. *Cardiovasc Res.* 2000;**47**:446–456. DOI: 10.1016/S0008-6363(00)00078-X.
- [163] Miranda-Rottman S, Aspillaga A, Pérez D, Vásquez L, Martínez A, Leighton F. 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.* 2002;**50**:7542–7547. DOI: 10.1021/jf025797n.
- [164] Falkenberg SS, Tarnow I, Guzman A, Mølgaard P, Simonsen HT. Mapuche herbal medicine inhibits blood platelet aggregation. *Evid Based Complement Altern Med.* 2012;**2012**:1–9. DOI: 10.1155/2012/647620.
- [165] Jofré I, Pezoa C, Cuevas M, Scheuermann E, Freires IA, Rosalen PL, de Alencar SM, Romero F. Antioxidant and vasodilator activity of *Ugni molinae* Turcz. (Murtilla) and its modulatory mechanism in hypotensive response. *Oxid Med Cell Longev.* 2016. DOI: 10.1155/2016/6513416.