Advances in Polyphenol Research from Chile: A Literature Review

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Abstract: Certain countries have the privilege of diverse ecosystems that allow access to wide food availability. This fact carries an intrinsic diversity in bioactive compounds such as phytochemicals, especially polyphenols. The aim of this review is to summarize the advances in polyphenols research which have been conducted in Chile, with a focus on polyphenol-rich foods and health-related outcomes. In the first part, several studies that have analyzed food sources rich in polyphenols are presented. This is followed by a description of *in vitro* and *in vivo* studies from Chile that have evaluated the polyphenol compounds of Chilean foods or their extracts along with their biological activity or health effects. Most polyphenol studies in our search have an *in vitro* experimental design where mainly protective activities are tested. The antioxidant effect is remarkable in all studies. As well as discussing the future direction of dietary assessment and the approach to biomarkers in this field, currently, additional emphasis and research investment are necessary to explore more native foods with an added value.

Keywords: food sources; polyphenol-rich foods; diet; health; Chile

1. Introduction

Two decades ago, phenolic compounds were primarily studied for their essential role in plant physiology. However, the focus has shifted to their potential beneficial effects on human health. Polyphenols, also called "phenolics" or "poly-phenolic compounds", are a large family of phytochemicals comprising at least 10,000 different structures.[1]

They are products of the secondary metabolism of plants.[2] Their main classification depends on their carbon skeleton, characterized by having one or more hydroxyl groups attached to a benzene ring, the number of phenolic rings, and other compounds such as organic or carboxylic acids. Phenolic compounds are classified into four main classes: flavonoids, phenolic acids, lignans and stilbenes[3], and these classes into more than 20 subclasses.[3, 4] In nature, most polyphenols occur in the form of glycosides, esters or polymers, while aglycones are rarely found, except for flavanol monomers.[2] These structural variations cause differences in their bioavailability and biological activity.[5]

Polyphenols are widely distributed in plant-based foods, especially fruits, vegetables, whole-grain cereals, cocoa and beverages (such as coffee, tea and wine).[2, 4] The health effects of these foods are partially attributed to their content of polyphenols. Evidence from cellular and animal models has increased the recognition of their antioxidant, anti-inflammatory, and anti-carcinogenic properties, among others.[4, 6] Moreover, several large epidemiological studies have associated polyphenol intake with a lower risk of all-cause mortality and various chronic diseases, such as cardiovascular diseases (CVDs), type 2 diabetes, osteoporosis, and neurodegenerative diseases.[5, 7] Furthermore, it has been suggested that polyphenol-rich foods play a positively role in gut microbiota and intestinal permeability.[8, 9]

Despite the fact that there is an increase in research into polyphenols, limitations in its dietary assessment methods, food composition databases, analytical procedures in foods and biological samples and validated nutritional biomarkers are still on a developing stage.[7, 10] Besides, more observational studies and clinical trials in humans are needed to define with accuracy recommended food intake based on physiological or pathological status. Furthermore, there is no clear reference recommendation for total polyphenol intake. The literature presents an approximate mean intake of 1 g/day with a range of 0.5-2 g/day.[11] Therefore, it would also be interesting to study variability across geographic areas where dietary patterns and their foods are different such as Latin America.[12] Although dietary polyphenols intake has not been estimated in Chile, an increasing number of studies have described the polyphenols profile of Chilean foods and its potential health benefits.[13, 14] Thus, we will present the advances in polyphenols research conducted in Chile, focusing on polyphenol-rich foods and health. The purpose of this review is to raise awareness and promote further research on polyphenols, especially on diet and health outcomes.

2. Methodology

A literature search of all studies published was performed using Web of Science (WoS) and PubMed and other databases (SciELO and Latindex) with the addition of other scientific papers of relevance found in web sources or in previously published reviews. In the first section (State of the art regarding polyphenols studies in Chile), the common search terms and strategy used for the studies selection were: "Food" OR "Food sources" OR "Diet" OR Polyphenol-rich foods" OR/ AND "Health" AND "Polyphenols" AND "Chile". In the second section (Future directions), other terms were considered: "Polyphenols dietary" OR "Dietary assessment" OR "Biomarker" OR "Metabolomics". After that an additional search was conducted in main foods found: "Strawberry" OR "Raspberry" OR "Currants" OR "Maqui" OR "Murta" OR "Blueberry" OR "Luma" OR "Calafate" OR "Red Wine" OR "Mango" OR "Chañar" OR "Avellana" OR "Apple" OR "Corn" OR "Quinoa" OR "Chagual" OR "Seaweed" OR "Baylahuen" OR "Pichi" OR "Boldo".

According to first section, main inclusion criteria: i) studies analyzing phenolic compound from foods; (ii) studies reporting an association between phenolic compounds and health outcomes; iii) studies from Chile; iv) studies published from August 2005 to December 2020; and v) English or Spanish languages. A total of 501 studies were screened and 224 were excluded based on title and/or abstract. The full text of eligible studies (n = 277) was read; 185 studies were excluded because not meeting the inclusion criteria or not of interest/pertinent. At the end of the selection process, 92 papers were included. The results are presented by food categories according to the selected studies considering their contribution of phenolic compounds, dietary consumption, among others.

3. State of the art regarding polyphenols studies in Chile

3.1. Geography and food availability

Chile is a long and narrow South American country with a huge diversity of landscapes (Figure 1). This offers a large biodiversity of plant-based foods rich in polyphenols, such as fruit, nuts, berries and spices.[11] Other foods such as vegetables, legumes, cereals are less rich in polyphenols but they are widely consumed and still constitute major source of polyphenols in the human diet.[12]

The Andes mountains form a natural north to south barrier that creates a dry climate in the north, warm in the center and humid and high-rainfall climate in the south. In the northern region of Chile vegetables, dry fruits, grapes and mangoes are some of the most common foods produced.[15] The central region of Chile presents a Mediterranean climate, and is the traditional wine-making region of the country.[16] In the central and southern parts of Chile, blueberries, grapes, prunes, dehydrated apples, hazelnuts and other native berries are produced and consumed by the population.[17, 18] Patagonia is the austral zone of Chile. In this zone there are cultivation of up to 28 species of native berries.[14]

From a food market perspective, Chile ranks among the top 10 global exporters of food, supplying more than 190 countries worldwide.[18] The main exported foods are processed fruits and vegetables (such as nuts, dehydrated and frozen fruits, juices and canned fruits and vegetables), followed by fresh fruits, seafood, and other foods and beverages like wines.[18]

3.2. Dietary pattern and its relationship with polyphenols food sources

The dietary pattern of a country or region is influenced by multiple factors, including the environment, culture, socioeconomic factors, education, climate, among others. This dietary pattern may be compromised by the country's food security. Chile produces a vast quantity and variety of fresh food, however this is not reflected in its population's consumption. Therefore, unfortunately, a country's dietary pattern may not be positively associated with its food production and availability.[19]

The National Survey of Food Consumption in Chile (ENCA) has shown alarming figures where only 5% of the population has meet dietary intake healthy guidelines.[20] According to the Chilean dietary guidelines, only 52% of the population achieved the fruit and vegetables recommendations, with an average consumption of 168 g and 227 g per day, respectively. The most frequently consumed vegetables are tomatoes, lettuce and carrots, while the most common fruits are bananas, apples and oranges. In the case of pulses, only 25% meet the recommendation of two times per week (1 serving = 60-80 g dry). As regards to the consumption of fats and oils, the consumption of foods rich in saturated fats (such as butter and paté) and polyunsaturated vegetable oils (such as sunflower, corn and canola) predominates. In the cereals group, bread is the most consumed food and there is an important increase on the intake of breakfast cereals in school children and teenagers. The intake of these food groups differ markedly by age, socioeconomic level and geographic area of residency.[21] For example, the reported consumption of fruits and vegetables was lower at the low socioeconomic level and in the southern area. Therefore, this is useful for developing targeted interventions through public policies.

The last Chilean National Health Survey (CNHS) conducted in 2017 showed that only 15% of the Chilean population achieved the recommendation of consuming five portions of fruit and vegetables per day.[22] Furthermore, only 40% and 60% declared having consumed fruit and vegetables, respectively, in the previous seven days. In the case of pulses, 24.4% of Chileans achieved the dietary guidelines (two portions per week), which was very similar to the findings from the ENCA. Moreover, in the CNHS only 24% of the sample were regular whole-grain consumers (three times a week or more).

Thus, the CNHS showed that there is a low contribution from plant food sources rich in polyphenols, such as fruit, vegetables and pulses. Additionally, a multicenter study in Latin America concluded that the food habits in terms of health are far from reaching dietary recommendations and the main sources of foods are ultra-processed, rich in energy, sugars and fats, and poor in phytochemicals.[19, 23] Certainly, the relevance of consuming polyphenol-rich foods is increasing, especially given that the United Nations General Assembly has declared 2021 as the International Year of fruit and vegetables.

The Mediterranean diet has become very popular worldwide due to the large body of research that supports its positive health effects.[24] One of its characteristics is being a good source of polyphenols.[25] The Mediterranean diet could be adopted by the Chilean population, especially because central Chile, also known as the country's agricultural heartland, represents one of the five world's Mediterranean ecosystems.[26] Moreover, there are many traditional Chilean dishes, such as charquicán, porotos granados, caldillo de congrio, pebre, among others, incorporate food ingredients and cooking techniques that are commonly used in the Mediterranean diet.[27, 28]

3.3. Polyphenols in Chile: Food Sources

This section describes the polyphenols profile of food sources according to evidence reported in the literature. We present total phenolic content (TPC) expressed as mg gallic acid equivalents (GAE)/g by food sources. (Table 1).

3.3.1 Berries

Some native South American berries have been studied recently, including varieties of strawberry *(Fragaria chiloensis* (L.) Mill.), currants (*Ribes* spp.), maqui (*Aristotelia chilensis* Molina Stuntz), murta *(Ugni molinae* Turcz), raspberries (*Rubus* spp.), calafate (*Berberis microphylla* G.Forst.) and pomegranate (*Punica granatum* L.).[14, 29-32]

F. chiloensis is endemic to southern Chile and can also be found in some parts of Peru and Ecuador. Cheel et al.[33] studied several strawberry varieties, including *F. chiloensis*, *Fragaria vesca* L. and Fragaria × ananassa (Duchesne ex Weston) Duchesne ex Rozier. They found that *F. vesca* had the highest TPC with 268.1 mg GAE/100 g fresh fruit and the total flavonoid content ranged between 30.0 mg to 123.2 mg quercetin equivalents/100 g fresh fruit, being higher for *F.* × *ananassa*.[33] The main anthocyanins found in strawberries were pelargonidin 3-glucoside, followed by cyanidin 3-glucoside and pelargonidin 3-rutinoside.[34] It is important to highlight that polyphenolic compounds and concentrations are different among species and subspecies of strawberries.[30, 34, 35] Finally, the main phenolic compounds of the white strawberry (*Fragaria chiloensis* subsp. *chiloensis*) were identified as ellagitannins, ellagic acid, quercetin, kaempferol and isorhamnetin derivatives.[36]

Raspberry *(Rubus geoides* Sm.*)* called "frambuesa silvestre" grow from southern Chile to Patagonia and Tierra del Fuego. The main phenolic compounds identified are flavonols, anthocyanins and tannins, among others.[29, 37-39] The raspberry extract showed a higher total antioxidant capacity than other berry species from the genus Ribes (e.g. *Ribes magellanicum* Poir. and *Ribes cucullatum* Hook. & Arn.) and *Gaultheria mucronata* (L.f.) Hook. & Arn.[40] Also, it has a similar antioxidant capacity to black prunes and bing cherries.[41]

Jimenes-Aspee et al.[31] investigated the phenol content and total antioxidant capacity of South American currants *(Ribes* spp.*)*. They are native species found in southern Chile and Argentina. Ripe fruits of *R. cucullatum*, *R. magellanicum*, *Ribes punctatum* Ruiz & Pav. and *Ribes trilobum* Meyen were evaluated. They discovered around 60 polyphenols: 23 anthocyanins, 13 hydroxycinnamic acids (HCAs) and 23 flavonols.[31] The currants *R. magellanicum* and *R. punctatum* are the most abundant wild species in Chile.[42]

The fruit *A. chilensis* is commonly known as maqui berry, Chilean blackberry or "maqui," and is a common edible berry from central and southern Chile.[43] The polyphenolic compounds of maqui have been studied by different authors and they are rich in anthocyanins, especially delphinin and cyanin.[44-54] The polyphenolic profile of maqui identified eight anthocyanins, ten flavonols and ellagic acid.[55] A recent review reported and summarized the literature about the content of bioactive compounds of maqui.[13]

U. molinae is a shrub that produces a fruit called murta, murtilla, Chilean cranberry or Chilean guava. It is a native fruit from Chile (between the VII and X regions) and from certain regions of Argentina and Bolivia.[13] Several studies described its phenolic content and total antioxidant capacity[37, 50, 56-60], especially of the leaves that are used to prepare both herbal teas and liqueurs.[49, 61-64] They contain different classes of polyphenols such as phenolic acids, flavanols, flavonols and hydrolyzable tannins.[13] The flavonoid composition in murta leaves is approximately three times higher than that in murta fruit.[61] Nevertheless, the amount of flavonols observed in murta fruit is double the amount in both maqui and calafate fruits.[65]

The blueberry (*Vaccinium corymbosum* L.) is the most important commercial variety. Chile is the world's second largest exporter with 107,229 tons produced principally in the south of the country.[66, 67] Blueberries are one of the richest sources of anthocyanins, which contribute up to 60% of the total polyphenolics in ripe blueberries.[70] The content of flavonoids, total phenols and the total antioxidant capacity of several varieties have been reported in Chilean samples[29, 30, 37, 41, 50, 53, 60], and have also been included in the Web-based database www.portalantioxidantes.com.[41] One study investigated the most complex anthocyanin profile in six Chilean berries, identifying 23 compounds in the highbush Brigitta blueberry variety. [58] The lowbush Elliot variety has a higher antioxidant capacity than the highbush Brigitta variety (8,869 vs 5,539 µmol TE 100 g fresh weight). Also, the TPC and ORAC values of traditional berries such as blackberry and raspberry are similar to those of the Elliot blueberry variety.[41, 69] However, native berries such as maqui and calafate have a superior antioxidant capacity (19,850 and 25,662 µmol TE/100 g fresh weight, respectively).[41] Those results from Chile were found to be consistent with other studies that have analyzed the content of polyphenols and their antioxidant capacity in lowbush and highbush blueberry varieties.[68, 70]

The native berries from arrayán are located in the south of Chile and Argentina. These berries have been employed to prepare "chichi," a Mapuche fermented beverage.[60] We found a scarcity of research about these berries of the genus *Luma*: *Luma apiculata* (DC.) Burret and *Luma chequen* (Molina) A.Gray. To date, 27 phenolic compounds have been identified, including 7 tannins, 15 flavonol derivatives and 5 anthocyanins[71], as well as new anthocyanin compounds.[60] The phenolic content of *L. apiculata* is higher than that reported for other berries such as raspberry (*Rubus idaeus* L) and blackberry (*Rubus fruticosus* L).[71] Moreover, arrayán berries present a high antioxidant capacity such as in murta (*U. molinae*).[58] Another study showed that the ripening process is crucial, observing that later ripening stages provides a higher level of antioxidant and polyphenolic content.[72]

Finally, *B. microphylla* and *Berberis darwinii* Hook., also known as calafate or barberry, are native to the Patagonian area of Chile and Argentina.[14] Calafate fruits are dark purple, black, or bluish. The polyphenol profile of calafate is characterized by high concentrations of anthocyanins, flavonol and HCA derivatives (17.81

μmol/g fresh weight (FW), 1.33 ± 0.54 μmol/g (FW) and 2.62 μmol/g (FW), respectively).[50, 73] The most abundant individual polyphenols are anthocyanin 3-glucoside conjugates, and the quercetin and isorhamnetin derivatives for flavonols.[50, 53, 58, 73-75] The calafate is ranked as the highest total antioxidant capacity consumed fruit in South America.[41, 60]

3.3.2. Grapes and Wine

Various studies have evaluated the TPC in seed, skin, whole and juice from of grapes varieties (*Vitis vinifera* L.).[76, 79] A study demonstrated that four varieties of Chilean grapes studied represent an important source of antioxidants, considering TPC, anthocyanins and phenolic acids. Authors showed that antioxidant capacity and phenolic content are higher in blue grapes cv. Autumn and Ribier compared to red grapes cv. Crimson and Red.[80] In Chile, around 70% of the world's red wine varieties are cultivated, such as Cabernet Sauvignon, Carménère and Syrah, and others.[16] Cabernet Sauvignon is one of the most important cultivars in Chile and is commonly blended with other varieties to produce wines. One study evaluated the content of four monovarietal red wines: CS, CR, Merlot (CM) and Cabernet Franc (CF) and their blends. They found that the anthocyanin content ranged from 342.7 to 707.8 mg malvidin equivalent (ME)/L^{-1} and the tannin content ranged from 1700.8 to 2254.7 catechin equivalent (CE)/L^{-1}.[81] The phenolic compounds of Carignan noir grapes have recently been characterized.[82, 83] This minor variety, especially those from Maule region in Chile, has had an important resurgence. Martinez-Gil et al.[82] identified 17 individual anthocyanins (total content ranging from 1046.3 to 1591.2 mg/kg), nine individual flavonol compounds, six individual flavanols and three individual HCAs. Climate is one of the most important factors affecting berry maturity and can influence flavonoid content.[83] Furthermore, the temperature impacts the composition and quality of grapes.[84] Anthocyanins and TPC have a positive association with exposure to sunlight.[85] Another study of the Carignan grape from the

Maule region obtained similar results, supporting the influence of the production zone and the year of harvest on the polyphenol content.[16] In general, the polyphenol profile of grapes and wines across the world shows similarities in their TPC, with a high level of anthocyanins (malvidin-3-*O*-glucoside), phenolic acids (gallic acid), stilbenes (resveratrol) , flavanols (catechins) and some flavonols (myricetin and quercetin).[86-88] Also, it is important to mention that white wine has lower TPC than red wine.[81, 89] Furthermore, the variety of grape, the ripening, the production, and environmental and geographic factors influence the chemistry and antioxidant capacity of wine and can also determine its origin.[90]

3.3.3. Fruits, vegetables and other food sources

In the Atacama Desert in the north of Chile, local mangoes and fruit lemons are cultivated. Mango de Pica (*Mangifera indica* L.) Cv. piqueño is six to seven times smaller than the Tommy Atkins mango.[91] These both types of mangoes are the main mango varieties cultivated and consumed in the north of Chile. The total antioxidant capacity in the edible pulp of the mango de Pica is twice as big as that of the Tommy Atkins mango fruit cultivated in the same area of Chile. In this investigation, 21 phenolic compounds were detected and tentatively characterized in mango fruits from northern Chile.[91]

Geoffroea decorticans (Hook. & Arn.) Burkart (chañar) is a tree which produces a brown sweet drupe fruit. The fruit extracts and derivate products such as arrope are commonly prepared.[92] This spice is widely distributed in the arid lands of the Andes plateau, including the north of Chile.[93] The total antioxidant capacity, TPC and flavonoid content of Argentinean *G. decorticans* have been reported.[94] In samples from Chile, 53 phenolic compounds were identified, mainly flavonol glycosides and procyanidins.[93]

The native nuts of *Gevuina avellana* Molina are mainly obtained from the south of Chile. Pino-Ramos et al.[95] found that hydroxybenzoic and HCAs were the main phenolic compounds in nuts. Likewise, they reported low levels of TPC and antioxidant capacity compared to other fruits.[95] It is documented that the roasting process negatively affects the composition of polyphenols and the total antioxidant activity of nuts.[98] Moreover, a recent untargeted metabolomics study showed that different hazelnut cultivars of diverse origins present distinct polyphenol profiles in the same geographical area.[17]

Legume seeds are rich in many nutrient including protein, starch, dietary fiber, among others. Particularly, a study examined the TPC and phenolic compound composition in immature seeds of fava bean (*Vicia faba* L.) varieties cultivated in Chile and they found different quantities of procyanidins, prodelphinidins, flavonols and flavones.[97]

Lutz et al.[69] evaluated TPC and antioxidant capacity (AC) of fruits and vegetables. All foods were harvested at their mature state from Aconcagua Valley (Valparaiso, Chile). The berries, eggplant (*Solanum melongena* L.) and spinach (*Spinacia oleracea* L.) exhibited the highest TPC, as expected the dehydrated process generated a major amount of TPC in all foods.[69] One of the most consumed fruits worldwide and in Chile is the apple.[20, 98] The total polyphenol content was studied in various varieties in Chile: Granny Smith, Royal Gala, Red Delicious, Pink Lady and Fuji.[29, 99, 100] Similar contribution of polyphenols were presented in the most common apple varieties, being higher in the snack apples in dry form.[98, 101]

Phenolic content in cereals such as corn (*Zea mays* L.) may be important natural sources in the total polyphenol dietary intake. Phenolic profile of 33 Chilean native corn accessions were evaluated and the main phenolic acids detected were ferulic and p-coumaric acids.[102] Quinoa (*Chenopodium quinoa* Willd.) is a pseudocereal and traditional Andean plant whose seeds are resistant to adverse environmental conditions.[103] Also, the quinoa seeds are recognized for their high nutritional value, fiber content and polyphenols compounds such as genistein and daidzein.[103-105] It has been shown to have good results in antioxidant capacity under field conditions and under controlled conditions in the context of water restriction.[106]

Puya chilensis Molina, known as "chagual," is an endemic plant growing in the central valley and coastal mountains of Chile. Traditionally, chagual is used as a food plant for the preparation of salads. There is only one study describing its phenolic compounds, identifying 14 flavonoids and 12 HCAs.[107] The phenolic-enriched extract (PEE) content is up to 10 times higher in the meristem than in the leaves; however, the meristem showed a higher total antioxidant capacity than the leaves.[107]

Seaweeds, or macroalgae, are very rich in many bioactive compounds, including polyphenols. Six edible seaweeds collected in Chile were studied. The main extractable polyphenols were HCAs, hydroxybenzoic acids and flavonols.[108] Other Chilean seaweeds study considered the *Durvillaea antarctica* known as "cochayuyo" have a most higher content of polyphenols and antioxidants activity than the other red and brown algae analyzed.[109]

Regarding medicinal plants, the aerial parts of *Haplopappus* spp., known under the traditional name "baylahuen," are used as herbal teas in Chile and Argentina. Schmeda-Hirschmann et al.[110] identified 27 phenolics compounds in these infusions, including 10 caffeoyl quinic and feruloyl quinic acid derivatives and 17 flavonoids. *Fabiana imbricata* Ruiz & Pav*.,* a Patagonian medicinal plant known under the names of "pichi" or "pichi romero," also contains a rich diversity of bioactive compounds, including phenolic acids, coumarins, flavonoids and terpenes, among others.[111, 112] *Peumus boldus* Molina a Chilean tree traditionally known for infusions of boldo leaves from which at least 40 phenolic compounds have been identified.[113, 114] Furthermore, edible fruit of the boldo has also been studied and has less antioxidant activity and phenolic content than other fruits like berries.[115]

There are other foods, especially fruits that are grown in Chile and South America with an interesting profile of polyphenols and TPC such as papaya (*Vasconcellea pubescens* A.DC.) [116], cactus prickly pear (*Opuntia* spp.)[117], copao (*Eulychnia acida* Phil.)[118, 119], algarrobo (*Prosopis* spp.)[120], Loquat (*Eriobotrya* *japonica* (Thunb.) Lindl.)[121], "Chaura" (*Gaultheria Pumila*) and (*Gaultheria poeppigii* DC.) [122, 123], Nalca (*Gunnera tinctoria* (Molina) Mirb.)[124] and honey[125] (Table 1).

It is worth mentioning that in various food sources of the same species, certain variations in the concentration of phenolic compounds may be found. These variations are explained by the genotype, environmental factors such as soil quality, temperature and altitude, geographic location, season, harvest (i.e. stage of maturity), fertilization farming method and conservation process.[55, 126-129] In addition, some variation may be due to the differences in the analytical methodology applied. Finally, given the wide variety of climates and foods cultivated in the South America and especially in Chile, further studies assessing both the content and the profile of polyphenols in native foods across the country are warrantes.[130]

3.4. Polyphenols and health

A description of *in vitro and in vivo* studies from Chile that have evaluated the phenolic compounds in Chilean foods or their extracts with their biological activity and potential health benefits is presented below. We present the main biological activities and potential health benefits (Table 2).

3.4.1. Berries

One study showed positive effects on the gastric adenocarcinoma cell line through the activation of intracellular antioxidant responses by PEE from native Chilean species of strawberry (*F. chiloensis* subsp. *chiloensis*), raspberry (*R. geoides*) and currant (*R. magellanicum*).[131] However, Thomas-Valdes et al.[132] showed a decrease in bioactivity and phenolic profiles after simulating the gastrointestinal digestion of white strawberries (*F. chiloensis* subsp. *chiloensis*). Despite these changes, the digested PEE still exhibited some antioxidant activity.[132] Raspberry extract may induce cytoprotective effects and intracellular antioxidant responses in human gastric cells. [38, 131] Moreover, the supplementation of white strawberry in mice showed a positive effects on oxidative and inflammatory responses after a liver injury induced by lipopolysaccharide.[133]

Burgos-Edwards et al.[134] also studied polyphenols from Chilean currants *(Ribes spp.)* and demonstrated their positive effect on antioxidant capacity and metabolic syndrome-associated enzymes (α-glucosidase). The fermented PEE of Chilean wild currants increased the antioxidant capacity compared to the non-digested PEE. HCAs and anthocyanins were the major phenolic compounds found in the PEEs before fermentation.[134]

Several years ago, Miranda-Rottmann et al.[135] studied the maqui, *A. chilensis*, which is rich in anthocyanins, and reported positive results in preventing low-density lipoprotein oxidation and improving antioxidant capacity.[135] Since then, various *in vitro* and *in vivo* studies have linked maqui phenolics with their high antioxidant capacity[49], inhibition of adipogenesis and inflammation[53, 136-139], prevention of oxidative stress[54, 139], anti-cancer[140] and anti-diabetic effects[45, 49, 141], and photoprotective[142], antibacterial[55], neuroprotective[143, 144] and cardioprotective[137, 145] properties. Despite their gastrointestinal effects, phenolic compounds still have great potential as antioxidant agents[146], although the antioxidant role of polyphenols in humans is still limited. [147] However, some studies have shown that maqui berry extract (Delphinol®) and its anthocyanin content can simultaneously reduce fasting blood glucose and insulin levels in prediabetic conditions.[148, 149] Thus, two studies are currently investigating the feasibility of powdered maqui extracts for food products and supplements.[150, 151]

The polyphenol compounds in both the leaves and fruits of murta (*U. molinae*) have shown potential protective effects against chronic diseases (e.g. human cancer types) through their biological activities.[56] *In vitro* studies showed that murtilla fruit and leave extract has antioxidant, protection oxidative damage, vasodilator and antimicrobial properties.[152-156] An experimental assay showed that murta juice retains a high proportion of polyphenols but there are differences when comparing *in vitro* gastrointestinal digestion processes.[157] A recent review extensively describes the biological activities of murta.[158]

A recent review presented wide-ranging evidence of the positive health effects of blueberries, from in vitro to human studies, including both observational and clinical trials.[68] In Chile, blueberries showed the highest inhibition of lipoperoxidation in human erythrocytes among six Chilean berries.[58] Due to the scientific knowledge that exist and the high level of production of blueberries in the zone, it is strongly recommended to develop strategies to promote its local consumption.

Extracts of calafate (*B. microphylla*) fruits showed antioxidant, anti-inflammatory and anti-cancerous properties, as well as the ability to enhance insulin resistance.[53, 139, 159-161] Also, a potent vasodilator action was observed in a rat arterial mesenteric bed bioassay.[162] Human cell models are demonstrating an anti-inflammatory response.[163] Finally, a randomized clinical trial evaluated the effect of a concentrated berry juice on postprandial oxidative stress and antioxidant status. In healthy volunteers, it decreased postprandial oxidative stress in a context of digestion and thermal processing of the red meat.[164]

3.4.2 Grape and wine

The common grape vine (*Vitis vinifera* L.) along with is by-products as wine production as part of a Mediterranean-style diet have shown to improve antioxidant defenses and, consequently, reduce oxidative damage caused by a Western diet.[165]. However, studies are still lacking to determine whether the detrimental impact of alcohol in wine beverages seem to be partly counterbalance by the Mediterranean diet and their antioxidant properties related to polyphenols.[166] Indeed, the use of emergent technologies to extract added value compounds from grape and wine by-products are being development.[167]

The byproducts of wine production process like grape pomace represent a rich sources of phenolic compounds.[168] One study evaluated the effect of wine grape pomace flour on components of metabolic syndrome in human adults.[169] After 16-weeks of longitudinal intervention, the consumption of flour as a functional food ingredients to a regular diet, improves some components of metabolic syndrome.

Resveratrol is a natural compound present in some fruit and wine products that have well-known antioxidant and anti-proliferative properties. It has been suggested that it plays a role in reducing cancer and diabetes risk, especially due to its inhibitory glucose uptake properties associated glucose transporter 1 (GLUT1).[170]

3.4.3. Other food sources

Reynoso et al.[94] presented some evidence about ethnomedical uses of *G. decorticans* and showed the antinociceptive action of this plant. Other studies that worked with samples of chañar fruits from Argentina and Chile observed that PEEs have inhibitory effects against pro-inflammatory and metabolic syndrome associated-enzymes.[92, 93]

A recent study evaluated the effect of polyphenolic extracts of the avocado (*Persea americana* Mill.) peel on human fecal microbiota in the presence of high protein content. These extract are rich in proanthocyanidins (PAs) and they improve colonic homeostasis and have anti-inflammatory propieties.[171, 172] Similarly, other studies also observed protective effects of PAs from other fruit sources against high *p*-cresol exposure in colonic epithelial cells[173], and a decreasing deleterious effect of sulfide on colonocyte respiration.[174]

The medicinal use of native plants in Chile has a long history and tradition and is based on South Andean indigenous cultures. However, to date, there is only one official scientific guideline that describes the medicinal, agronomic and culinary properties of Chilean native plants.[175] The knowledge gleaned and advances realized on plant infusions and their composition, especially polyphenols, mean that suggestions can be forwarded about their possible effects on health.[111, 176-179] One plant in particular has been extensively studied: boldo (*P. boldus*), employed in traditional medicine with leaf infusions and other derivates.[180, 181] A few years ago, some researchers associated it with many beneficial effects on gastrointestinal, liver and renal diseases, especially due to its anti-inflammatory and antioxidant activities.[180, 182] Many studies attribute its beneficial effects to an alkaloid named "boldine," specifically in relation to improving kidney damage.[183, 184] However, various studies have demonstrated the important role of flavonoids, phenolic compounds and catechin in regard to their medicinal properties.[113, 185] In an *in vivo* study, a boldo infusion reduced the oxidative damage induced in mice.[186] Another study suggested that boldo extract has a potent anti-*Helicobacter pylori* properties, directly linked to the presence of catechin-derived PAs.[187]

One study showed the antioxidant and anti-diabetic activities (i.e. pancreatic lipase and α-glucosidase inhibition) of Latin American fruits such as maqui, cape gooseberry and papaya, which are rich in bioactive compounds.[43] Other studies showed the beneficial effect of several native fruits and berries such as açaí (*Euterpe oleracea* Mart.), Andean blackberry (Rubus Glaucus Benth), Andean blueberrie (*Vaccinium floribundum* Kunth), acerola (*Malpighia emarginata* DC.), noni (*Morinda citrifolia* L.) which present antioxidant, anti-diabetic, anti-inflammatory and anti-cancer activities.[43, 136]

The majority of these studies are *in vitro*. The antioxidant effect is remarkable and several researchers recommend to moving forward and using them in *in vivo* studies, especially in humans. [7, 188, 189] They also promote the creation of new functional foods. Overall, we need more prospective studies in human to confirm these potential health effects.

4. Future directions: dietary assessment approach

4.1. Polyphenol dietary intake

Although the intake of dietary polyphenols has not been estimated in Chile, various countries have assessed the total intake of polyphenols and especially flavonoids.[7] Europe and the US are leading the research conducted on polyphenols. However, to the best of our knowledge, there have been few studies in Latin America were found.[7]

We did, however, find two articles from Brazil.[190, 191] Miranda et al.[190] estimated from 24-hour dietary recall (24-HDR) an average intake of 377.5 ± 15.3 mg/d total polyphenols; the main polyphenol classes were phenolic acids and flavonoids, and the highest food contributor to polyphenol intake overall was coffee. However, in another study using multiple 24-HDRs, the average total intake of polyphenols was 1198.6 mg/d, including aglycones (533.7 mg/day).[191] These results are closer to the range reported in other populations, including France (1193.6 mg/d, 820 mg/day as aglycone equivalents).[192] Moreover, in other European regions, the mean total polyphenol intake was much higher such as in Denmark with 1786 mg/day in men and 1626 mg/day in women, and in Poland with 1755 mg/day in men 1727 mg/day in women.[4, 193]

In Argentina, a study was carried out in a small sample of children aged between 6 and 12, which evaluated the intake of total polyphenols using an food frequency questionnaires (FFQ).[194] A low contribution of 412 mg/day was obtained, partly due to low fruit consumption. Also, in a large Mexican cohort of teachers a median polyphenol intake of 694 mg/day was found using a validated FFQ.[195] These results were comparable with the mean intake in Greece and Spain.[4] It is important to mention that polyphenol intake was also shown to be associated with age, sex, socioeconomic status, and ethnicity, with all of these factors being known to affect food choices.

Nonetheless, a Chilean study measured the phenolic content of the breakfast and lunch meals that delivered the Chilean National School Feeding Program. The total mean contribution of phenolic compound were 1.4 and 4.8 mg GAE/g in breakfast and lunch, respectively.[196] Currently, there is a lack of evidence in polyphenols content by meals, however, this study provides useful data of phenolic compounds in institutional meals which emphasizes the importance of providing legumes, wholegrain products, fruits and vegetables in meal events. Only one experimental study conducted on Italian older volunteers has described contributions of polyphenols meals content according to the sum of individual polyphenols, and has obtained similar results at breakfast and lunch, but important differences in snacks between the polyphenol-rich-diet and the control diet.[197] It is important to further investigate the role of meal events considering the type of sample according to demographic characteristics, methodological design (experimental method) and food sources related to the estimation of dietary polyphenols.

4.2. Dietary assessment and biomarker approach

The relationship between polyphenols intake and health outcomes has become a major research area in human nutrition. One of the most important challenges is to achieve an accurate estimation of polyphenol intake. For that purpose, it is important to employ a standardized process that uses an accurate food composition databases, and validated and reliable dietary assessment methods.[198]

There are two major global food composition databases for polyphenols: the United States Department of Agriculture (USDA) and the Phenol-Explorer (www.phenol-explorer.eu) databases.[199] The USDA released the first flavonoids database in March 2003 and currently has three updated databases on flavonoid, isoflavone and PAs aglycones in 2018.[200] Phenol- Explorer published its first version in 2009 and the last update was in 2015 including data on glycosides and esters of polyphenols and retention factors. [199, 200]

The most common technique used to quantify polyphenols is high-performance liquid chromatography (HPLC); it is currently combined with mass spectrometry but there are different analytical methods and that should be a variable to consider. Another difficulty associated with polyphenol content is the variability found in the food composition of each food, product or food recipe. This may encompass two stages: The first concerns production an takes into consideration the plant variety, geographical area, condition of cultivation and ripeness stage at harvest; and the second is about food storage and processing and mainly considers cooking techniques.[195]

The most common questionnaires used are 24-HDR, diet history interview and FFQ. All of them have some limitations that are inherent in each dietary assessment method, but the use of innovative technologies such as myfood24 may facilitate and improve this process.[201] We must also have a precise strategy for extracting and processing food data that ensures high data quality, as well as adequately combining these with the polyphenol databases selected.[202] Standardization of the procedures for the quantification of polyphenols is key to a better validation and comparison of data.[10]

Measuring markers in biological samples can be an objective way to estimate polyphenol intake. This methodology could reinforce or complement classic dietary assessment methods. The benefits associated may reduce biases related to dietary questionnaires and also take account of interindividual variations in the bioavailability of polyphenols in specific tissues.[12]

Biomarkers must be validated to ensure that they accurately reflect the exposure. Intra and interindividual differences in polyphenol metabolism should also be considered. The choice of urine samples could have some advantages such as having higher polyphenol concentrations than plasma and the fact that they are less invasive, among others[198, 203] The limitations and challenges of biomarkers considering validated analytical methods in population studies, these methods should be highly sensitive and specific to be compatible with the low concentrations commonly found in biological samples.[12] Recent developments in analytic techniques and in metabolomics allow the measurement of large sets of polyphenols in blood and urine.

The development of research areas related to dietary patterns and biomarkers, along with metabolome-wide associated studies, will allow us a better understanding of the impact of diet on individual and population health. Recent studies propose the interaction of the food metabolome with an exposure perspective.[204] In addition, essential data on genetics, metabolomics, metagenomics, lifestyle and clinical data, among others, are required for precision nutrition at the individual level.[205] The analysis of biological big data and the creation of metabotypes profiles will enhance the investigation of dietary biomarkers and personalized nutrition.[206]

The perspective and future of food metabolomics, including the polyphenols metabolome, is exponentially increasing and required from a complex network of support and resources from different areas of knowledge such as health, nutrition, bioinformatics, chemistry and omics sciences.[207] This integration contributes to a better understanding of the relationship between human diet and health.[208]

This review summarizes a significant number of studies investigating polyphenols in foods and their protective effects on health outcomes, particularly in Chilean native berries with a high TPC, antioxidant activity and where mainly anti-inflammatory, anti-diabetic and cardio-protective properties are demonstrated. However, this information is still very limited and has several challenges. The Latin American region with its diverse climates provides a great opportunity for research in dietary polyphenols. Besides, the intake of dietary polyphenols has not been estimated in Chile. Therefore, it is essential to increase research on food sources rich in polyphenols, including the development of functional foods with value added, and their estimation in regard to dietary intake and its impact on human health.

The advancement and the integration of the research results on different scientific design scales, including observational and intervention studies, promoting a transnational science which will be essential for future health recommendations. The challenges of positioning, evaluating and quantifying the dietary intake of polyphenols will require different phases of work. These phases will involve resources in the academic and scientific research fields associated with public and private institutions. Generating more evidence will accelerate these challenges.

Consequently, further research should be conducted in order to determine whether the active promotion of adherence to a specific dietary pattern or polyphenol-rich food sources could improve health and decrease the risk of diseases, co-morbidities and mortality, especially in chronic diseases. Finally, Chile and Latin American countries should generate the necessary resources to systematically assess their population's eating patterns and thus support clinicians and policy makers in improving dietary guidelines and recommendations.

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Abbreviations

TPC: total Phenolic Content

PEE: phenolic-enriched extract

PAs: proanthocyanidins

24 HDR: 24-hour dietary recall

FFQ: food frequency questionnaires

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Figure 1. Map of Chile showing the zones and regions. Source: NordNordWest & Janitoalevic 2018, with slight modifications.

Table 1. Summary of the total phenolic content (mg GAE / 100g) by food sources, species, regions of Chile, origin and weight expressed.

Food (common name)	**Species**	**Region of Chile**	**Origin**	**Weight**	**Total Phenolic Content *(mg GAE / 100g)***	**Reference**
Strawberry (Frutilla)	*Fragaria × ananassa (Duchesne ex Weston) Duchesne ex Rozier*	O'Higgins	Fruit *cv. Camarosa*	FW[a]	210	[29]
		Valparaíso	Fruit cv. *Camarosa*	FW	630	[30]
			Fruit *cv. Sabrina*		650	
			Fruit *cv. Sabrosa*		850	
			Fruit *cv. Siba*		630	
		Biobío	*cv. Chandler*	FW		[31, 32]
			Whole fruit		230	
			Achene		3600	
			Thalamus		30	
	Fragaria chiloensis (L.) Mill.	N.A (Chile)	Whole fruit	FW	200	
			Achene		3600	
			Thalamus		37	
	Fragaria vesca L.	Los Ríos	Whole fruit	FW	268	
			Achene		1750	
			Thalamus		99	
	Fragaria chiloensis subsp. chiloensis	Biobío	Whole fruit	FW	106	
			Achene		4294	
			Thalamus		73	
		Biobío	Fruit	FW[a]	272	[36]
			Leaves		498	

Raspberry (Frambuesa silvestre)	*Rubus idaeus* L.	O'Higgins	Fruit	FW	295	[30]
				FW[a]	262	[29]
		Ñuble	Fruit	FW[a]	200	[37]
		Maule	Fruit	FW[b]	183	[38]
	Rubus geoides Sm.	La Araucanía			904	
		Aysén			347	
		Magallanes			531	
	N.A	N.A	Fruit	FW	380	[39]
Chilean Currant (Grosella)	*Ribes magellanicum* Poir.	La Araucanía	Fruit	FW - PEEs	393	[31]
	Ribes punctatum Ruiz & Pav.	Biobío			362	
		Aysén			326	
	Ribes cucullatum Hook. & Arn.	La Araucanía			389	
	Ribes trilobum Meyen	Maule			248	
Maqui	*Aristotelia chilensis* (Molina) Stuntz	Valparaíso	Fruit	FW	1230	[30]
		O'Higgins			1580	
		Maule			1500	
		La Araucanía			1370	
		NA (Chile)	Fruit	FW	1664	[41]
		O'Higgins	Fruit	FW	880	[44]
		Aysén	Fruit	FW	1970	[46]
		La Araucanía	Fruit	FW[a]	1222	

			Juice	FW	730	
			Juice	FW	911	[47]
		Maule	Fruit	FW	1620	[48]
		Valparaíso			1450	
		La Araucanía			1110	
		O'Higgins			1600	
		La Araucanía	Fruit Stem Leaves	FW[a]	1750 990 2640	[49]
		Biobío	Fruit	FW[b]	113	[50]
		Araucanía			75	
		Los Ríos			103	
		Biobío	Fruit	FW[a]	1300	[52]
		Los Ríos	Fruit	FW[a]	728	[53]
		Biobío	Fruit	FW[a]	1900	[55]
Murta –Murtilla	*Ugni molinae* Turcz	Los Lagos	Fruit ripe Fruit non-ripe	FW[a]	2360 1190	[37]
		NA (Chile)	Fruit	FW	863	[41]
		Araucanía	Fruits Stems Leaves	FW[a]	190 300 2925	[49]
		Biobío	Fruit	FW[b]	35	[50]
		La Araucanía			27	

		Los Ríos			32	
		La Araucanía	Fruit ripe	FW	210	[56]
			Leaves	DW[c]	18108	[57]
					27900	[62]
		Biobío	Fruit	FW[a]	179	[58]
		La Araucanía	Fruit S1 S2 S3 S4 S5	FW[a]	 401 706 149 157 237	[59]
		Biobío	Fruit	FW[a]	180	[60]
			Fruit Leaves	FW[a]	550 2220	[61]
		Biobío	Infusion (Leave)	FW[a]	40	[63]
		Valparaíso			65	
Blueberrie Highbush (Arandano)	*Vaccinium corymbosum* L.	Maule - Biobío	Fruit *cv. Legacy*	FW	620	[30]
			Fruit *cv. Aurora*		505	
			Fruit *cv. Brigitta*		610	
			Fruit *cv. Liberty*		670	
			Fruit *cv. Elliot*		840	
			Fruit *cv. Ozarkblue*		490	
		Ñuble	Fruit	FW[a]	490	[37]

		N.A (Chile)	Fruit	FW	262	[41]
			Fruit *cv. Brigitta*	FW	274	
			Fruit *cv. Aurora*	FW	392	
			Fruit *cv. Blue-crop*	FW	393	
			Fruit *cv. Blue-gold*	FW	497	
		Biobío	Fruit *cv. Blue-gold*	FW[a]	855	[72]
		La Araucanía	Fruit	FW[b]	17	[50]
		Ñuble	Fruit	FW[a]	734	[58]
		Los Ríos	Fruit	FW[a]	197	[53]
		Ñuble	Fruit *cv. Brigitta*	FW[a]	734	[60]
		Valparaíso	*cv. O´Neal* Fruit Dry Fruit	FW[a]	 236 6495	[69]
		O'Higgins	Fruit *cv. Duke*	FW[a]	240	[29]
Blackberry (Mora)	*Rubus ulmifolius* Schott	Valparaíso	Fruit *cv. Navaho* Fruit *cv. Prime-Jim* Fruit *cv. Prime-Jan*	FW	740 590 580	[30]
		O'Higgins	Fruit *cv. Cherokee*	FW[a]	333	[29]
	Morus nigra L.	Valparaíso	*cv. Cherokee* Fruit Dry Fruit	 FW[a] 	 351 12577	[69]

Arrayán	*Luma apiculata* (DC.) Burret	Biobío	Fruit	FW[a]	340	[58]
			Fruit	FW[a]	339	[60]
			Fruit Aerial	FW[a]	362 2210	[71]
			Fruit S1 Fruit S2	FW[a]	816 811	[72]
Chequén	*Luma chequen* (Molina) A.Gray	Biobío	Fruit	FW[a]	60	[58]
			Fruit	FW[a]	63	[60]
			Fruit Aerial	FW[a]	60 4020	[71]
Barberry (Calafate)	*Berberis microphylla* G.Forst.	N.A (Chile)	Fruit	FW	1201	[41]
		Aysén	Fruit	FW*	93.3	[50]
		Magallanes			78.4	
		Biobío	Fruit	FW[a]	1630	[58]
		Aysén	Fruit	FW	555	[73]
		La Araucanía			53	
		Magallanes			420	
		Biobío	Fruit	FW[a]	1502	[60]
		La Araucanía	Fruit	FW[a]	564	[75]
		Aysén			1146	
		Los Ríos	Fruit	FW[a]	336	[53]
Grapes	*Vitis vinifera* L.	Valparaíso	*cv. Red Globe* Skin Juice	FW[a]	 1232 28	[80]

			cv. Crimson Seedless Skin Juice *cv. Autumn Royal* Skin Juice *cv. Ribier* Skin Juice		 1254 28 2516 56 2439 50	
			cv. Cabernet S. Skin Ground grape Juice *cv. Pais* Skin Ground grape Juice	 FW	 220 160 15 80 50 10	[76]
		Metropolitana de Santiago	*cv. Cabernet S.* Skin Seed *cv. Carménère* Skin Seed	 FW	 140 1600 160 1770	[77]
			cv. Cabernet S.			[78, 79]

			Skin Seed *cv. Carménère* Skin Seed cv. Merlot Skin Seed *cv. Cabernet Franc* Skin Seed	FW	255 1813 305 2320 315 2173 260 2118	
Red Wine	*Vitis vinifera* L.	Metropolitana de Santiago	*cv. Cabernet S.*	FW	89	[81]
			cv. Carménère		92	
			cv. Merlot		80	
			cv. Cabernet Franc		101	
White Wine	*Vitis vinifera* L.	Metropolitana de Santiago	*cv. Sauvignon blanc*	FW	18	[79]
Pomegranate	*Punica granatum* L.	Valparaíso	Fruit *cv. Wonderful*	FW	390	[30]
		N.A	Fruit Juice	FW	105	[32]
Mango de Pica	*Mangifera indica* L.	Tarapacá	*cv. Piqueño* Pulp Peel	FW	 32.5 72.0	[91]
Mango Tommy Atkins			*cv. Tommy Atkins* Pulp Peel	FW	25.0 43.2	

Chañar	*Geoffroea decorticans* (Hook. & Arn.) Burkart	Atacama	Pulp	FW[c]	639	[93]
Chilean Hazelnuts (Avellana)	*Gevuina avellana* Molina	Maule	Raw Roasted	FW[a]- PEEs	2346 1932	[95]
		Ñuble	Raw Roasted		4140 4232	
		Biobío	Raw Roasted		4140 5658	
		Los Lagos	Raw		2484	
Hazelnuts (Avellana)	*Corylus avellana* L.	N.A (Chile)	Raw Roasted (160ºC) Roasted (180 ºC)	FW[a]	1328 397 455	[96]
Fava Bean	*Vicia faba* L.	Metropolitana de Santiago	Raw	FW	110	[97]
Corn/ Maize	*Zea mays* L.	Regions of Chile	Raw	FW[a]	45	[102]
Quinoa seeds	*Chenopodium quinoa* Willd.			FW[a]	140	[103]
		Ñuble	Field condition Controlled condition	FW	313 566	[106]
Apple	*Malus domestica* Borkh.	O'Higgins	*cv. Fuji* Pulp Peel *cv. Red Delicious* Pulp Peel	FW[a]	 160 421 168 536	[29]

			cv. Royal Gala			
			Pulp		115	
			Peel		344	
			cv. Granny Smith			
			Pulp		191	
			Peel		497	
			cv. Pink Lady			
			Pulp		38	
			Peel		268	
		Maule	*cv. Fuji*			
			Whole fruit		170	[99]
			Pulp		150	
			Peel		650	
			cv. Red Delicious			
			Whole fruit		220	
			Pulp		180	
			Peel		1150	
			cv. Royal Gala			
			Whole fruit		180	
			Pulp		150	
			Peel		610	
			cv. Granny Smith			
			Whole fruit		200	

			Pulp Peel *cv. Pink Lady* Whole fruit Pulp Peel		185 700 160 140 580	
		Metropolitana de Santiago	*cv. Fuji* Whole fruit Peeled fruit Dry fruit *cv. Royal Gala* Whole fruit Peeled fruit Dry fruit *cv. Granny Smith* Whole fruit Peeled fruit Dry fruit	FW	 100 90 360 120 100 390 140 110 370	[98]
		N.A	*cv. Fuji* Fruit Fruit Dry	FW	 57 503	[101]
		Valparaíso	*cv. Granny Smith* Fruit Fruit Dry	FW[a]	 91 5049	[69]

			cv. Red Delicious Fruit Fruit Dry		 143 4872	
Pepper Sweet	*Capsicum annuum* L.	Valparaíso	Red Vegetable Red Dry Vegetable Green Vegetable Green Dry Vegetable	FW[a]	63 5871 46 5464	
Carrot	*Daucus carota* subsp. *sativus* (Hoffm.) Arcang.		Vegetable Vegetable Dry		38 1957	
Eggplant	*Solanum melongena* L.		Vegetable Vegetable Dry		68 7998	
Spinach	*Spinacia oleracea* L.		Vegetable Vegetable Dry		83 5084	
Tomato	*Solanum lycopersicum* L.		Vegetable Vegetable Dry		12 5825	
Red Seaweeds	*Gracilaria chilensis*	Los Lagos	Raw	FW[a]	205	[108]
	Callophyllis concepcionensis				211	
Green Seaweeds (Sea lettuce)	*Ulva* sp.				246	

	Enteromorpha compressa				243	
Brown Seaweeds (Kayamo-nori)	*Macrocystis pyrifera*				189	
	Scytosyphon lomentaria				315	
Brown Seaweed (Cochayuyo)	*Durvillaea antarctica*	Los Ríos	Raw	FW[a]	148	[109]
Tea Baylahuen	*Haplopappus baylahuen* J.Rémy	Atacama	Infusion	FW[a]	35	[110]
	Haplopappus rigidus Phil.	Valparaíso	Infusion	FW[a]	17	
	Haplopappus deserticola Phil.	O'Higgins	Infusion	FW[a]	24	
Pichi Romero	*Fabiana imbricata* Ruiz & Pav.	Ñuble	Infusion	FW	12	[112]
Boldo	*Peumus boldus* Molina	Biobío	Infusion	FW[a]	69	[114]
Papaya	*Vasconcellea pubescens* A.DC.	Maule	Fruit	FW[a, c]	276	[116]

Copao	*Eulychnia acida* Phil.	Coquimbo	Fruit	FW	62	[118]
			Pulp Epicarp	FW[c]	608 469	[119]
Algarrobo (Flour)	*Prosopis chilensis* (Molina) Stuntz	Coquimbo	Flour	FW	1710	[120]
Loquat	*Eriobotrya japonica* (Thunb.) Lindl	Valparaíso	*cv. Golden Nugget* Fruit	FW[a]	60	[121]
Nalca	*Gunnera tinctoria* (Molina) Mirb.	Los Ríos	Plant	FW[a]	1202	[122]
Chaura	*Gaultheria poeppigii* DC.	La Araucanía-Los Lagos	Fruit	FW	395	[124]
Honey	Floral origin (types)	Valparaíso	Raw	FW	93	[125]

GAE: gallic acid equivalents; N.A: not available; FW: Fresh Weight; DW: Dry Weight; S: Season of harvest; PEEs: polyphenol-enriched extracts; cv: *cultivated variety*. [a] The fresh weight was obtained from dry weight by % standard moisture equation. The % moisture was obtained from original articles, USDA or another databases. [b] FC: Folin-Ciocalteu method. [c] The total phenolic content are expressed as mg GAE/100 g MeOH extract.

Table 2. Summary of study sample, biological activity and potential health benefits by food sources and species.

Food	Specie	Main polyphenolic groups	Material or subject of intervention (Type)	Biological activity and potential health benefits	Ref
Raspberry	*Rubus geoides* Sm.	Flavonoids Tannins Procyanidins	AGS cell PEE	Protective effect on AGS cells against oxidative. Increased the intracellular GSH content.	[38]
Strawberry	*Fragaria chiloensis* subsp. *chiloensis*	Anthocyanins Flavanols Phenolic acids	AGS cells Gastrointestinal fluid PEE	Decrease by > 50% in the total phenolic content at the end of the GID. Reduce antioxidant capacity after GID. Not significantly protecting AGS cells against H_2O_2-induced stress. GID decreases the inhibitory effect of α-glucosidase and lipase.	[132]
			Male Sprague-Dawley rats	Attenuated hepatic oxidative stress (> GSH/GSSG ratio). Inhibited inflammatory response.	[133]
Currant	*Ribes magellanicum* Poir. *Ribes punctatum* Ruiz & Pav.	Anthocyanins Flavanols Hydroxycinnamic acids	Human fresh fecal PEE	Fermented colonic might contribute to the prevention of high-blood glucose levels. Colonic fermentation induce changes in the phenolic profile. Anthocyanins and hydroxycinnamic acids was most affected.	[134]

				The antioxidant capacity was higher after 8 h fermentation in both species.	
Maqui	*Aristotelia chilensis* (Molina) Stuntz	Anthocyanins Proanthocyanidin Phenolic acids	Male C57BL/6J mice H4IIE and L6 cell	Improves hyperglycemia and insulin resistance.	[45]
			Fruit, leave and stems.	Inhibiting effects on α-glucosidase and α-amylase activity. Antioxidant activity.	[49]
			RAW264.7 mice cell 3T3- L1 cell mice cell	Prevention of macrophage activation. Improving effects on adipocytes apoptosis.	[53]
			Rat brain homogenates	Reduce oxidative stress. Antioxidant activity.	[54]
			HUVEC Cells	Oxidative stress protection. Antioxidant activity.	[135]
			RAW264.7 mice cell 3T3- L1 cell mice cell	Reduce adipogenesis and lipid accumulation in adipocytes. Anti-inflammatory effect in macrophages.	[136]
			Male Wistar rats RAW264.7 mice cell	Inhibitory effects on inflammatory. Antioxidant activity.	[138]

			C57BL/6 male mice RAW 264.7 cell Blood and fecal samples	Antioxidant and anti-inflammatory activities. Reduces immune stress. Regulates gut microbiota.	[138]
			RAW264.7 mice cell 3T3- L1 cell mice cell	Increased GSH/GSSG ratio. Prevented caspase-3 induction. Decreased MCP-1 gene expression. Improved IRS-1 phosphorylation.	[139]
			HT-29 and Caco-2 cell	Exhibited chemoprotective abilities on decreasing growth of cellular models. Inhibiting lipid peroxidation.	[140]
			C57BL/6J male mice	Improve insulin response. Decreased weight gain. Increased thermogenic activity.	[141]
			Male BALB/c mice Human keratinocyte (HaCaT) cells	Prevents inflammation in skin mice by UVB-induced method. Protects against the damage caused by UVB exposure.	[142]
			PC-12 cell mice **(**Sprague-Dawley**)**	Neuronal protection against amyloid $A\beta$ toxicity.	[143]

			Male Wistar rats	Protects heart from damage induced. Inhibiting lipid peroxidation. Antioxidant activity.	[145]
			36 prediabetic human adult subjects. Delphinol capsule (maqui berry extract).	Decrease fasting blood glucose and insulin levels.	[148]
			C57Bl/6J mice. Ten Sprague Dawley rats. Five STZ-Diabetic rats. Ten human adults.	Reduces the glucose absorption in intestine by interaction with sodium glucose co-transporter SGLT-1 in mice model. Decreases postprandial glucose levels and insulin in subjects with moderate glucose intolerance.	[149]
Murta	*Ugni molinae* Turcz	Anthocyanins Phenolic acids Ellagitannins	Murta Fruit. Escherichia coli. Salmonella enteric *(S. typhi)*	Antioxidant and antibacterial activities.	[56]
			Murta fruit and leave. Escherichia coli and Listeria onocytogenes.	Antioxidant capacity and antimicrobial activities.	[61]
			HUVEC-C Cells	Reduced oxidative stress. Inhibiting lipid peroxidation and anion superoxide production.	[152]

			Human gut bacterial	Prebiotic effect (lactobacilli and bifidobacteria).	[153]
			Staphylococcus A., Enterobacter A., Pseudomonas A., Candida A., Klebsiella, P.	Antimicrobial activity.	[154, 155]
			Human red blood cells	Protection against oxidative damage.	[156]
Blueberry	*Vaccinium corymbosum* L.	Anthocyanins. Phenolic acids.	Fruit	Antioxidant activity.	[30, 41]
			Human red blood cells	Inhibition of lipoperoxidation in erythrocytes.	[58]
Arrayán	*Luma apiculata* (DC.) Burret	Flavonol Anthocyanins Tannins	Male Sprague-Dawley rats (Aortic rings)	Protect endothelium-dependent vasodilation on hyperglycemia condition.	[71]
Barberry (Calafate)	*Berberis microphylla* G.Forst.	Anthocyanins Flavonols	RAW264.7 mice cell	Prevention of RAW264.7 macrophage activation.	[53]
			RAW264.7 mice cell 3T3- L1 cell mice cell	Improving effects on adipocytes apoptosis and insulin-sensitivity.	[139]

			C57BL6 obese mice	Attenuates the expression of pro-inflammatory markers and improve insulin sensibility in a diet-induced obesity model	[159]
			Human gastric and gallbladder (G415) cancer cell	Reduce in vitro viability and migration of AGS and G415 human cell lines.	[160]
			C57BL6 obese mice	Reduce body weight increase. Modulate inflammation. Promote energy expenditure.	[161]
			Male Sprague Dawley rats Endothelial cell from mesentery	Vasodilator and antioxidant activity.	[162]
Berries	*B. microphylla* G.Forst. *A. chilensis* (Molina) Stuntz *V. corymbosum* L.	Flavanols Anthocyanins Phenolic acids	THP-1 monocyte human cell Human pre-adipocytes cell	Inhibit inflammatory and oxidative response	[163]
Berries	*Rubus geoides* Sm. *Ribes magellanicum* Poir.	Flavonoids Anthocyanins Phenolic acids	AGS PEE (*Raspberry, Currant Strawberry)*	Protective effect in intracellular antioxidant responses. Increased levels of glyoxalase I and glutathione S-transferase.	[131]

	Fragaria chiloensis subsp. chiloensis				
	N.A other berries. *Ugni molinae* Turcz *Aristotelia chilensis* (Molina) Stuntz		Eleven healthy adult males Liquid mixture with berries *(cranberry, blueberry and blackberry)*	Decrease postprandial oxidative stress. Inhibiting lipoperoxidation reactions occurring at the stomach level.	[164]
Wine grape pomace flour	*Vitis vinifera* L. cv. Cabernet Sauvignon.	Anthocyanins	38 Human adults	Improves blood pressure and glycaemia. Reduce postprandial insulin levels and oxidative stress. Increased antioxidant defenses.	[169]
Chañar	*Geoffroea decorticans* (Hook. & Arn.) Burkart	Flavonoid Proanthocyanidin	PEE	Inhibition of pro-inflammatory enzymes (LOX, COX, sPLA2). Inhibition of the enzyme α-glucosidase, α- and lipase. Antioxidant activity.	[93]
Avocado	*Persea americana* Mill. cv. *Hass*	Flavanols	Human fecal samples HT 29 cell	Protective effect in reducing the production of ammonia and H2S. Increasing the production of butyrate and indole. Prevented the alterations in the intestinal permeability induced by high protein content.	[171]

			RAW 264.7 cell	Anti-inflammatory effect. Antioxidant activity.	[172]
Fruit mix	*Malus domestica* Borkh; Cranberry juice; *Persea americana* Mill. *Vitis vinifera* L. cv. Cabernet Sauvignon.	Flavonoids Anthocyanins Flavanols Phenolic acids	HT29 and Caco-2 cells PEE *(Apple, cranberries, avocado and grape)*	Protect cell integrity, intestinal barrier and mitochondrial function in abnormal p-cresol concentrations.	[173]
Seaweed (Cochayuyo)	*Durvillaea antarctica*	Total phenolic compounds	HT29	Antioxidant activity Anti-enzymatic capacity (α-glucosidase and α-amylase).	[109]
Boldo	*Peumus boldus* Molina	Flavanols	Human red blood cells	Inhibiting lipid peroxidation in erythrocytes.	[185]
			Males Mus musculus, Balb-C mice.	Prevents the oxidative hepatic damage induced by cisplatin.	[186]
			AGS cell Helicobacter pylori	Inhibition Helicobacter pylori adhesion to human gastric cells. Inhibiting the urease activity.	[187]

AGS: Human Gastric Adenocarcinoma cells; PEEs: polyphenol-enriched extracts; GID: Gastrointestinal digestion; GSH, reduced glutathione; GSSG, oxidized glutathione; MCP-1; monocyte chemoattractant protein-1; H4IIE: Hepatoma cell; L6: Myoblasts cell; RAW264.7: Macrophage cell; 3T3- L1: Adipocytes cell; HUVEC-C: Human Umbilical Vein Endothelial Cell; THP-1: Monocyte human cell; HT 29: Human colon adenocarcinoma cell; Caco-2: Colon cancer cells; LOX: Lipooxygenase; COX: Cyclooxygenase; sPLA2: Secretory Phospholipase A2.