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REVIEW ARTICLE

Polyphenols of *Carménère* Grapes

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Abstract: *Carménère* is the emblematic grape of Chile. Recent studies indicate that it has a different polyphenolic profile than other commercial varieties of grape among other factors, due to its long maturation period. The grape and wine of *Carménère* stand out for having high concentrations of anthocyanins (malvidin), flavonols (quercetin and myricetin) and flavanols (catechin, epicatechin and epigallocatechin). These compounds are related to the distinctive characteristic of *Carménère* wine regarding astringency and color. *In vivo* and *in vitro* models suggest some positive effects of these polyphenols in the treatment and prevention of chronic diseases, such as atherosclerosis and cancer. Therefore, there is a high level of interest to develop scalable industrial methods in order to obtain and purify *Carménère* grape polyphenol extracts that could be used to improve the characteristics of wines from other varieties or produce nutraceuticals or functional foods for preventing and treating various chronic diseases.

Keywords: *Carménère*, polyphenols, flavonols, anthocyanins, flavanols, bioactives.

1. INTRODUCTION

How people eat has drastically changed over the recent years; nutritional foods associated with wellness and health are growing in importance [1]. These foods contain bioactive compounds which help in the prevention and treatment of various chronic diseases [2]. For example, it has been shown that a diet rich in polyphenols helps in preventing various oxidative stress related diseases like cancer, and several cardiovascular and neurodegenerative diseases [3].

Polyphenols are bioactive compounds naturally present in fruits and vegetables, which are characterized by their huge antioxidant capacity. In fact, it has been demonstrated that an average intake of 1g/day of polyphenols is 10 times better than the consumption of vitamin C and 100 times better than vitamin E and carotenoids in protecting body tissues against oxidative stress agents [3-6].

From a chemical point of view, these compounds can be classified into two main groups: flavonoids (flavonols, anthocyanins and flavanols) and non-flavonoids (stilbenes and phenolic acids) [7, 8]. The latter are characterized by a structure of a single ring of 6 carbon atoms, while flavonoids have two rings of 6 carbon atoms.

Grapes are an excellent source of different polyphenols (~2-3 mg GAE/g). Most of these compounds are concentrated in the skin (flavonols and anthocyanins) and seeds (flavanoles) of grapes berries [9].

In addition to their health benefits, grape polyphenols play a key role in the sensory quality of wines, especially in reds, due to their impact on color and astringency [10-12].

Polyphenols are a highly heterogeneous and complex family of compounds (monomers, oligomers and polymers) that present several interactions with other organic compounds. These interactions include hydrogen bonds, esterifications, glycosylations and hydrophobic interactions [7]. All of them explain their biological activities in the human body and their sensorial effects in foods.

Several grape varieties have been identified to produce high quality wines with a specific polyphenol profile. In this sense, *Carménère* is the emblematic grape of Chile; its long maturation period (~170 days) after flowering favors the accumulation of polyphenols in the skin and reduces tannin levels in the seed of the grape berry [13-16].

Between 1997 and 2015, the surface planted with *Carménère* grape in Chile has increased from 330 to 10,732 ha [16]. The production of red wine from this variety has reached 70 million L/year (~9% of the Chilean wine production) [17]. Consequently, it is estimated that 30,000 TM of grape pomace of *Carménère* is generated each year in Chile [16, 17].

Wines derived from this variety have high concentrations of flavanols, anthocyanins and flavonols, such as quercetin and myricetin, malvidin and epigallocatechin, respectively [18, 19]. These polyphenols are related to the distinctive characteristics of the *Carménère* wine [10, 12].

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This paper compiles information about the most abundant polyphenolic compounds identified to date in the *Carménère* grape. In addition, some technological, sensory and bioactive properties associated with them are discussed.

2. POLYPHENOLS OF *CARMÉNÈRE*

In *Carménère* grapes, the molecular weight of polyphenols varies according to their degree of polymerization [8]. For example, the tannins or flavanols that confer the bitterness and astringency to wine have molecular weights between 500 and 3,500 kDa [8, 10, 20]. Similarly, anthocyanins with molecular weights higher than 5,000 kDa have been reported [21].

Polyphenols are distributed on the *Carménère* grape's skin and seed, as can be observed in Table **1**. Anthocyanins are the major components in the skin (~ 42%), while flavanols are major compounds in the seeds (~ 52%) [00, 0.].

Table 1. Distribution of polyphenols in *Carménère* grapes.

Location	Compounds	%
Skin	Anthocyanins	42.3
	Flavonols	0.3
	Flavanols	0.3
	Phenolic acids	0.1
Seed	Flavanols	52.0
	Phenolic acids	5.0

%: Expressed in terms of the total polyphenolic compounds found in the skin and seeds of *Carménère* grapes [18, 19, 22, 23].

The average content of total polyphenols in the skin and seeds of the *Carménère* grape is 1.1 ± 0.2 and 16.6 ± 2.8 mg GAE/g, respectively [18, 19]. In addition, wines from this variety contain between 2.23 and 2.86 g GAE/L [24]. The content of total polyphenols, anthocyanins and tannins distinguish *Carménère* from other commercial varieties like *Cabernet Sauvignon* (Table **2**) [25, 26]. However, it is important to note that the wine polyphenolic profile depends also on the agricultural and oenological practices, as well as on the intrinsic characteristics of the environment [25, 26]. Therefore, it is difficult to compare the polyphenolic content of a variety with respect to another. Here we consider the relative concentration of the various compounds (polyphenol profile) to highlight the benefits of a particular variety.

Given the complexity of grape polyphenols, previous studies with *Carménère* have focused on its monomers to differentiate and relate its polyphenolic profile to the particular characteristics of *Carménère* wine [18, 19, 24]. Although this variety has wide polyphenolic diversity between flavonols, anthocyanins and flavanols, this review will focus only on the compounds that differentiate *Carménère* from other grape varieties.

2.1. Flavonols

These compounds (Fig. **1a-1f**) are located in the *Carménère* grape skin and accumulate during the ripening period [18, 27]. The most common flavonols conjugates in grapes are the 3-*O*-glycosides as glucoside, galactoside and rutinoside [28, 29]. In wine, flavonols are in the form of aglycones or conjugates with free anthocyanins [30].

Figure **2** shows the concentrations of flavonols which are found in *Carménère* grape's skin such as quercetin-3-*O*-glucoside, myricetin-3-*O*-glucoside, quercetin-3-*O*-galactoside, kaempferol-3-*O*-glucoside and kaempferol-3-*O*-galactoside [31, 32]. These polyphenols are the most important antioxidants at a cellular level, especially quercetin [33].

The *Carménère* grape's skin has high concentrations of quercetin-3-*O*-glucoside (6.5 ± 1.6 mg/kg) and myricetin-3-*O*-glucoside (2.4 ± 0.3 mg/kg) compared with other varieties of grapes, such as *Merlot* and *Cabernet Sauvignon* (Fig. **3**).

Red *Carménère* wines have high concentrations of quercetin and myricetin [34-36]. A recent study found that in red wines the ratio of total quercetin and total myricetin in *Carménère* is higher than in *Cabernet Sauvignon* [30]. The concentration and type of flavonols present in grapes are important factors to improve and stabilize the color in red wines, due to their ability to interact with anthocyanins through copigmentation reactions (hydrophobic interactions) [35]. The characteristic of the color in red wines can be assessed through the CIELAB analysis. This method expresses color in terms of brightness, hue, and saturation, where L* represents the brightness, and a and b are chromatic coordinates [37, 38]. For example, the copigmentation in red wine

Table 2. Polyphenols content comparing *Carménère (*CM) with *Cabernet Sauvignon (*CS).

Description	Skin		Seed	
	CM	CS	CM	CS
Total Polyphenols (mg GAE/g)	1.1±0.2 [18]	0.8±0.3 [18]	16.6±2.8 [18, 19]	17.5±4.3 [19, 22]
Total Tannins (mg GAE/g)	2.8±0.4 [18]	3.0±0.1 [18]	32.9±3.9 [18, 19]	36.9±9.1 [19, 22]
Total Anthocyanins (mg ME/g)	0.9±0.2 [18]	0.5±0.1 [18]	- -	--

GAE: gallic acid equivalent, ME: malvidin-3-O-glucoside equivalent.

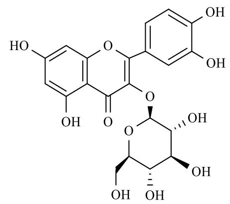

Fig. (1a). Quercetin-3-O-glucoside.

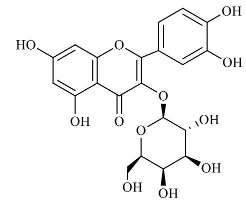

Fig. (1b). Quercetin-3-O-galactoside.

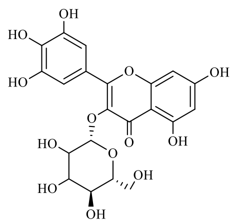

Fig. (1c). Myricetin-3-O-glucoside.

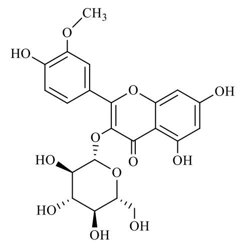

Fig. (1d). Isorhamnetin-3-O-glucoside.

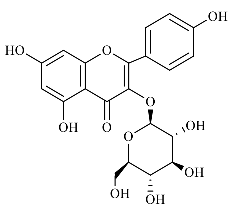

Fig. (1e). Kaempferol-3-O-glucoside.

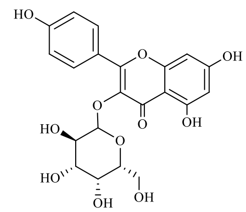

Fig. (1f). Kaempferol-3-O-galactoside.

Fig. (1a-1f). Chemical structures of flavonols.

as a result of the interaction between malvidin-3-*O*-glycoside and quercetin-3-*O*-glucoside, reduces brightness by 25%, with chromatic parameters for a and b of -3.43 and +7.64 respectively; this generates an intense bluish red in the wine [36].

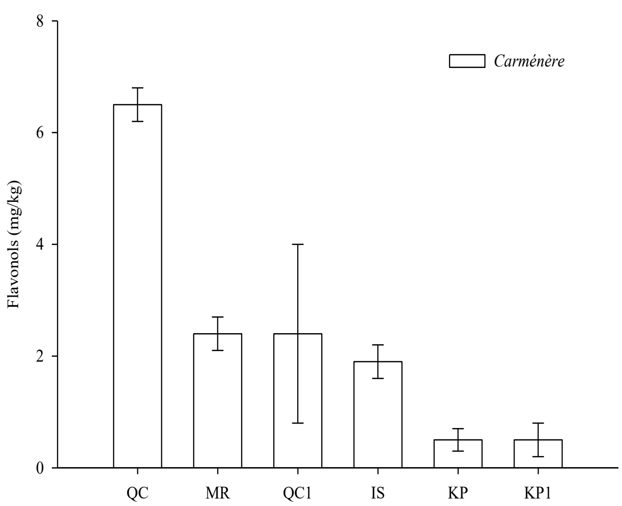

Fig. (2). Flavonols content in *Carménère* grape skin. QC: quercetin-3-*O*-glucoside, MR: myricetin-3-*O*-glucoside, QC1: quercetin-3-*O*-galactoside, IS: isoramnethin-3-*O*-glucoside, KP: kaempferol-3-*O*-galactoside, KP1: kaempferol-3-*O*-glucoside [18, 31, 32].

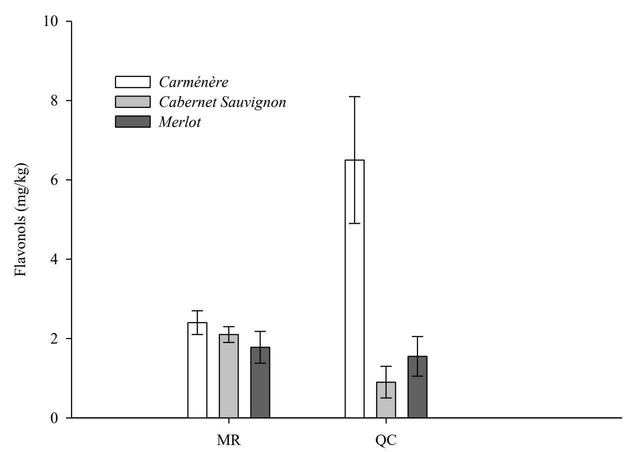

Fig. (3). Flavonols content in grape skins of *Carménère, Cabernet Sauvignon* and *Merlot.* QC: quercetin-3-*O*-glucoside, MR: myrecetin-3-*O*-glucoside [18, 31, 32].

2.2. Anthocyanins

Anthocyanins are found in the skin of *Carménère* grapes. They consist of anthocyanidins (aglycones) glycosylated with different sugars (glucose, galactose, arabinose and xylose) and esterified by different acids (acetic, coumaric and caffeic) [9, 31]. Malvidin, cyanidin, petunidin, delphinidin and peonidin are the most abundant anthocyanidins (Fig. **4a-4n**) found in

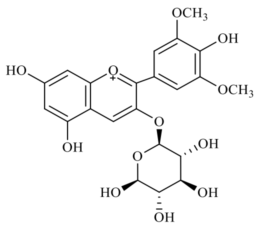

Fig. (4a). Malvidin-3-O-glucoside .

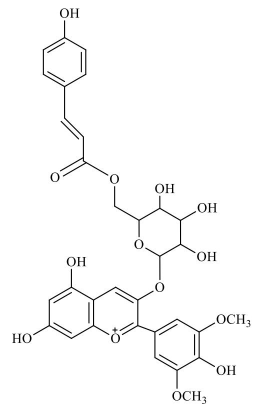

Fig. (4b). Malvidin-3-O-(6-coumaroyl)glucoside .

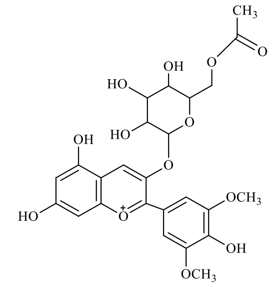

Fig. (4c). Malvidin-3-O-(6-O-acetyl)glucoside .

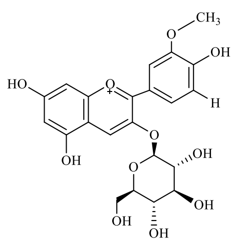

Fig. (4d). Peonidin-3-O-glucoside.

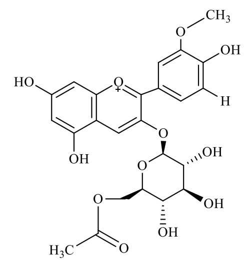

Fig. (4e). Peonidin-3-O-(6-O-acetyl)glucoside.

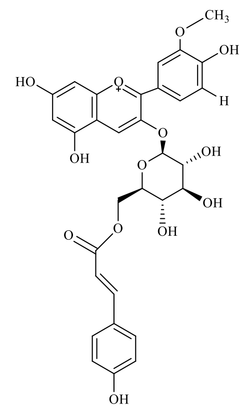

Fig. (4f). Peonidin-3-O-(6-O-coumaroyl)glucoside.

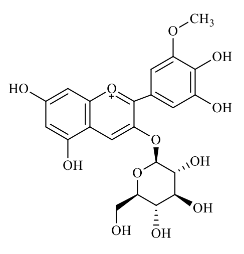

Fig. (4g). Petunidin-3-glucoside.

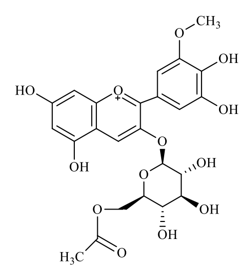

Fig. (4h). Petunidin-3-(6-O-acetyl)glucoside.

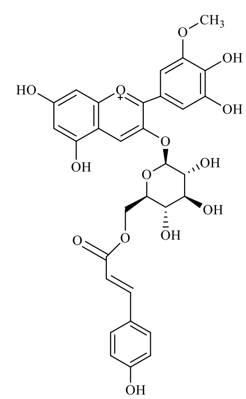

Fig. (4i). Petunidin-3-(6-O-coumaroyl)glucoside.

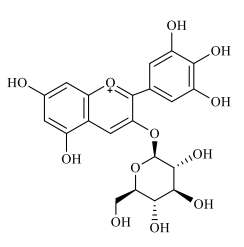

Fig. (4j). Delphinidin-3-O-glucoside.

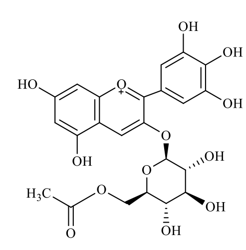

Fig. (4k). Delphinidin-3-O-(6-O-acetyl)glucoside.

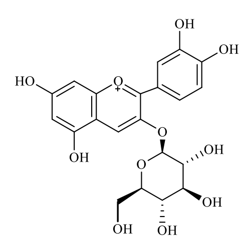

Fig. (4l). Cyanidin-3-O-glucoside.

Fig. 4. (contd).

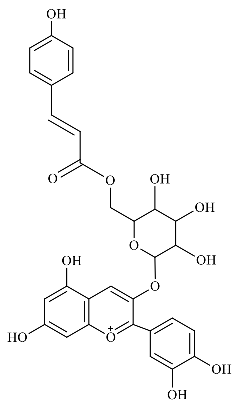

Fig. (4m). Cyanidin-3-O-(6-O-coumaroyl)glucoside.

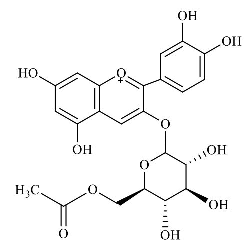

Fig. (4n). Cyanidin-3-O-(6-O-acetyl)glucoside.

Fig. (4a-4n). Chemical structures of anthocyanins.

Carménère anthocyanins [16, 28, 29]. So far, 18 anthocyanins have been identified in *Carménère* grape skin, including monoglucoside anthocyanins, acetyl monoglucosides, coumaryl monoglucosides, caffeoyl monoglucosides and feroloil monoglucosides (Fig. **5**).

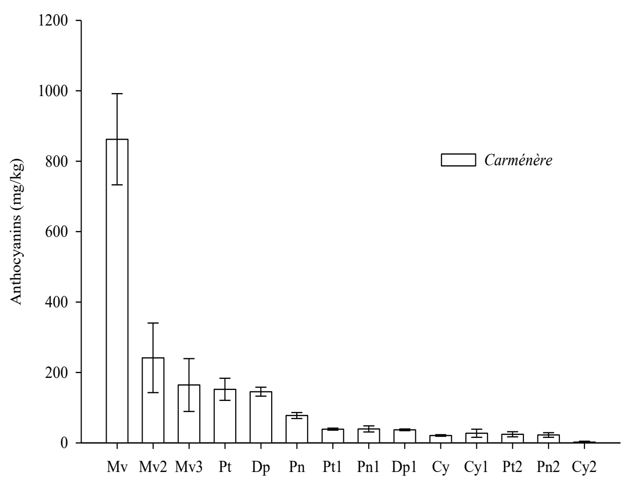

Fig. (5). Anthocyanins content in *Carménère* grape skin. Mv: malvidin-3-*O*-glucoside, Mv2: malvidin-3-*O*-(6-*O*-acetyl)glucoside, Pt: petunidin-3-*O*-glucoside, Dp: delphinidin-3-*O*-glucoside, Pn: peonidin-3-*O*-glucoside, Mv3: malvidin-3-*O*-(6-*O*-coumaroyl) glucoside, Pt1: petunidin-3-*O*-(6-*O*-acetyl)glucoside, Pn1: peonidin-3-*O*-(6-*O*-acetyl)glucoside, Cy: cyanidin-3-*O*-glucoside, Dp1: delphinidin-3-*O*-(6-*O*-acetyl)glucoside, Cy1: cyanidin-3-*O*-(6-*O*-coumaroyl)glucoside, Cy2: cyanidin-3-*O*-(6-*O*-acetyl)glucoside, Pn2: peonidin-3-*O*-(6-*O*-coumaroyl)glucoside, Pt2: petunidin-3-*O*-(6-*O*-coumaroyl)glucoside [18, 31, 44].

Anthocyanins are the pigments responsible for the color in red wines [7]. The color of these compounds depends on the number of hydroxyl and methoxy groups in their chemical structure. For example, higher hydroxylation degrees produce displacements towards blue hues while higher methoxylation degrees produce red colorations [39]. Therefore, the color in red wines is related to six anthocyanidins, such as cyaniding (red-orange), peonidin (red), delphinidin (bluish red), pelargonidin (orange) petunidin and malvidin (bluish red) [39, 40].

The *Carménère* grape, unlike other commercial varieties, such as *Cabernet Sauvignon* and *Merlot,* has high concentrations of malvidin-3-*O*-glucoside (862.21 mg/kg) (Fig. **6**). This compound is the major anthocyanin in grapes and wines. Hence, several studies assessed the co-pigmentation in red wines through interaction between malvidin-3-O-glucoside and other polyphenols (flavanols and flavonols) [36, 41, 42]. This type of interaction enhances between 30 and 50% the color intensity in aged red wines that can be quantified by the copigmentation constant (K_1). This constant measures the absorbance (nm) as a result of the association between two compounds [42]. Several studies have found that the interaction between malvidin and quercetin has high levels of copigmentation (K_1 = 2900 ± 1300 L/mol) compared to other polyphenols such as catechin (K_1 = 90 ± 20 L/mol) and proanthocyanidins (K_1 = 330 ± 30 L/mol) [36, 42, 43].

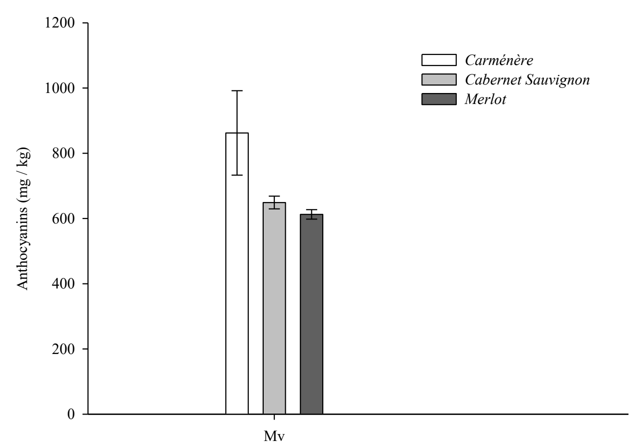

Fig. (6). Mv: Malvidin-3-*O*-glucoside content in grape skins of *Carménère, Cabernet Sauvignon* and *Merlot* [31, 44, 45].

2.3. Flavanols

Flavanols (Fig. **7a-7k**) are present in the *Carménère* grape's skin and seeds, as monomers and condensed tannins

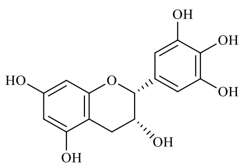

Fig. (7a). (-)-Epigallocatechin.

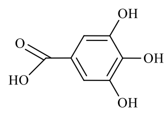

Fig. (7b). Gallic acid.

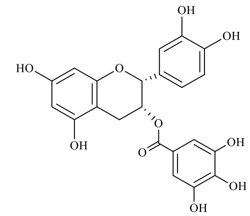

Fig. (7c). (-)-Epicatechin-3-O-gallate.

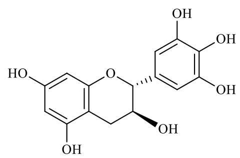

Fig. (7d). (+)-Gallocatechin.

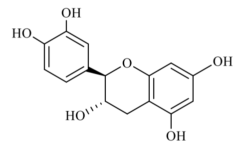

Fig. (7e). (+)-Catechin.

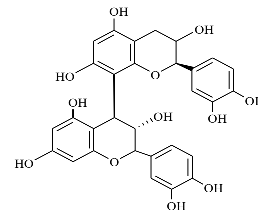

Fig. (7f). Catechin-(4,8)-catechin.

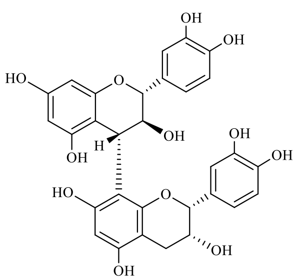

Fig. (7g). Catechin-(4,8)-epicatechin.

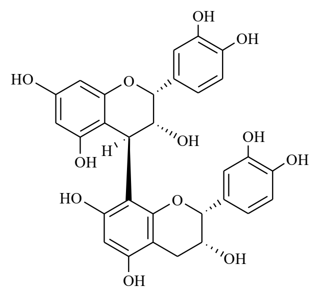

Fig. (7h). Epicatechin-(4,8)-epicatechin.

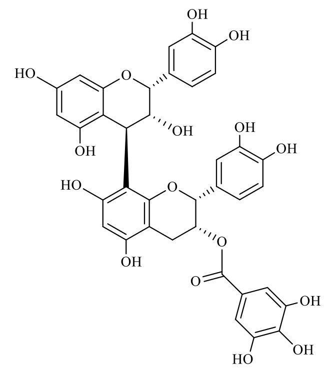

Fig. (7i). Epicatechin-(4,8)-epicatechin-3-O-gallate.

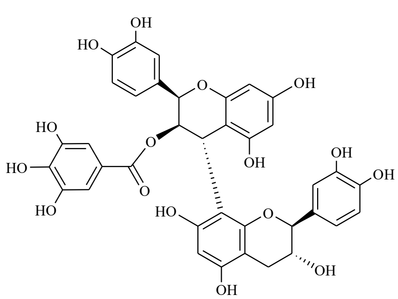

Fig. (7j). Epicatechin-3-O-gallate-(4,8)-catechin.

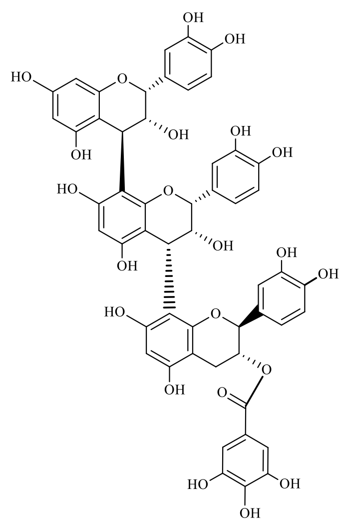

Fig. (7k). Epicatechin-(4,8)-epicatechin-(4,8)-catechin-3-O-gallate.

Fig. (7a-7k). Chemical structures of Flavanols (skin and seed).

(proanthocyanidins) in the form of simple dimers, or complex molecules (oligomers and polymers) [18, 19]. The major proportion of these compounds is found in the seed (~75%) [22].

The most abundant monomers in the *Carménère* grape's seed are (+)-catechin and (-)-epicatechin; whose concentrations are shown in Fig. (**8**). Several studies have reported the presence of proanthocyanidins in the form of dimers and trimers in the seed such as epicatechin-(4β-8)-epicatechin, catechin-(4α-8)-catechin, catechin-(4α-8)-epicatechin-3-O-gallate, among others (Fig. **8**) [18, 19, 22]. These compounds are generally dimers and trimers of catechin and epicatechin [46]. The flavanols in *Carménère*'s seed are galloylated with gallic acid (~13.8%) [23, 46]. This particular interaction between flavanol and gallic acid is responsible for the astringency and sensory perception in red wines [23, 47]. It has been shown that these galloylated flavanols interact with the proline reach proteins of human saliva, forming aggregates that contribute to wine astringency and bitterness [46, 48, 49].

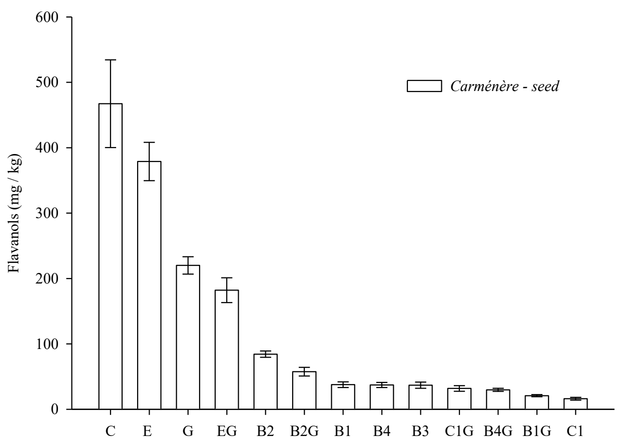

Fig. (8). Flavanols content in *Carménère* grape seed; C:(+)-catechin, EC:(-)-epicatechin, G: gallic acid, PB4: catechin-(4α-8)-epicatechin, PB2: epicatechin-(4β-8)-epicatechin B3: catechin-(4α-8)-catechin, B1: epicatechin-(4β-8)-catechin, B4G: catechin-(4α-8)-epicatechin-3-*O*-gallate, B1G: epicatechin-3-*O*-gallate-(4β-8)-catechin, B2G: epicatechin-(4β-8)-epicatechin-3-*O*-gallate, C1: epicatechin-(4β-8)-epicatechin-(4β-8)-catechin, C1G: epicatechin-(4β-8)-epicatechin-(4β-8)-catechin-3- *O*-gallate [18, 19, 22].

Skin flavanols include (-)-epigallocatechin, (+)-gallocathechin and (+)-catechin, as well as proanthocyanidins with high degree of polymerization (Fig. **9**). These proanthocyanidins are generally formed by catechin and epigallocatechin monomers [50]. Unlike seed flavanols, skin flavanols have a low percentage of galloylation (~1.9%) [23, 50].

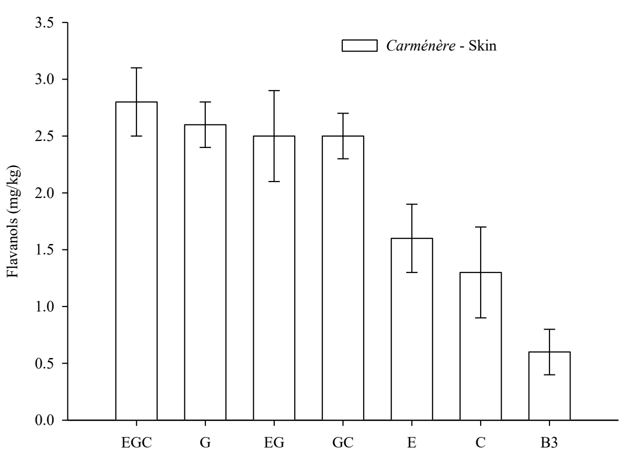

Fig. (9). Flavanols content in *Carménère* grape skin; EGC:(-)-epigallocatechin, G: gallic acid, EG:(-)-epicatechin-3-O-gallate, GC:(+)-gallocathechin, C:(+)-catechin, B3: catechin-(4α-8)-catechin [18, 22].

Compared to other commercial varieties such as *Merlot* and *Cabernet Sauvignon*, the *Carménère* grape's skin has high concentrations of epigallocatechin rich proanthocyanidins (Fig. **10**). Hence, the ratio of proanthocyanidins between seeds and skin is around 2, while in other commercial varieties such as *Merlot* and *Cabernet Sauvignon*, these ratios vary between 3 and 10 [23]. This particular characteristic distinguishes the sensory properties of *Carménère* wines from other varieties. A recent study found, through a scale of 0 to 10, that the level of astringency in *Carménère* wines is less than that of *Cabernet sauvignon*, with average scores of 5.3 and 6.0 respectively (p <0.03, LSD 5%) [23]. Red wines with high concentrations of tannins rich in epigallocatechin present low astringency, since these tannins do not form aggregates with the proteins of the human saliva [46, 51, 52].

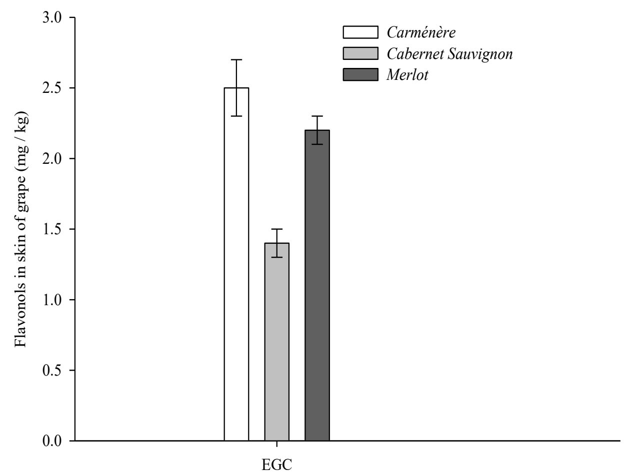

Fig. (10). EGC: Epigallocatechin content in grape *Carménère, Cabernet Sauvignon* and *Merlot* [18, 22, 45].

3. BIOACTIVE POLYPHENOLS FOUND IN *CARMÉNÈRE*

The chemical structure of polyphenols would determine some biological properties such as antioxidant activity and specific interactions with cell receptors that can be identified as the mechanisms responsible for their potential health benefits (Table **3**).

Several *in vivo* and *in vitro* studies have shown that most abundant *Carménère* polyphenols (*e.g.* malvidin, quercetin, myricetin and epigallocatechin) possess important biological activities (Table **3**). For example, *in vitro* studies performed in rat hearts have shown that malvidin, the major *Carménère* polyphenol, reduces mammalian myocardial contractility and induced coronary vasodilation [53]. These results evidence the potential health benefits of malvidin, as a human cardioprotective agent like resveratrol and cyanidin. Similarly, epigallocatechin and myricetin have been associated not only with the promotion of bone regeneration but also with the inhibition of cancer at *in vitro* and *in vivo* assays [54-56]. The biological activity responsible for these benefits seems to be specific for each polyphenol, as can be observed in Table **3**. Additionally, all these compounds exhibit anti-inflammatory effects both for *in vitro* and *in vivo* studies. Therefore, the extraction of these polyphenols from *Carménère* pomace could be considered a

Table 3. Potential health benefits of *Carménère* polyphenols. Main biological effects *in vitro* and *in vivo.*

Compounds	Potential Health Benefits	Biological Activity	References	
			in vitro Studies	*in vivo Studies*
Malvidin	Cardio-Protective Effects:	Modulates myocardial and coronary performance.	[53]	
		Regulates the activity of nitrous oxide synthetase enzymes.	[57]	
		Positive effect against lipid oxidation.	[57]	[63]
	Anti-Inflammatory Effects:	Inhibits macrophage activation in the blood.	[58]	[58]
		Attenuates the TNF-α-induced inflammatory responses in endothelial cells.	[59-61]	
	Anti-Carcinogenic Effects:	Mediate the cytotoxicity through the arrest of the G2/M phase of the cell cycle and by induction of apoptosis.	[60]	
		Inhibited the growth of HL60 human leukemia cells through the induction of apoptosis.	[62]	
Myricetin	Anti-Inflammatory Effects:	Inhibits the production of pro-inflammatory mediators through the suppression of NF-κB in LPS-stimulated RAW264.7 macrophages.	[64, 65]	
	Anti-Carcinogenic Effects:	Exerts potent anti-proliferative and pro-apoptotic effects on K562 human leukemia cells.	[66]	
	Bone Effects:	Inhibits osteoclast formation, and shows an effect in preventing alveolar bone loss.	[54]	[54]
Quercetin	Anti-Allergenic Effects:	Inhibits the release of histamine, IgE-mediated.	[67]	
	Anti-Inflammatory Effects:	Antioxidant and protective effect against gastric ulceration.		[72]
		Ability to suppress NO production in LPS-stimulated macrophage RAW 264.7 cells.	[68]	
		Interact synergistically with resveratrol contributing to counteract inflammation of the skin, and resulting in tissue repair and wound healing.		[73]
	Anti-Carcinogenic Effects:	Inhibits cell growth and induction of apoptosis in H460, A549 and H1299 lung cancer cells.	[69,70]	
		Inhibits the growth of HCT116 cancer cells which caused apoptosis in the cells.	[62]	
		Interact synergistically with resveratrol and ellagic acid in the induction of apoptosis and reduction of cell growth in human leukemia cells (MOLT-4).	[71]	
Epigallocatechin	Anti-Carcinogenic Effects:	Inhibits strongly the growth of breast cancer cell lines (MCF-7 and MDA-MB-231) due to an induction of apoptosis.	[74]	
	Bone Effects:	Effective in promoting osteogenic differentiation in bone formation.	[56, 55]	

good option to develop nutraceutical and functional food products.

4. CARMÉNÈRE GRAPE POMACE AS A SOURCE OF VALUABLE POLYPHENOL EXTRACTS

Carménère grape is produced especially for the elaboration of red wine; the remnants of this process, such as skin, stems and seed, are known as grape pomace. This agroindustrial residue contains between 60% and 65% of the grape polyphenols after red wine production [75]. The concentration of phenolic compounds in the grape pomace depends on the wine processing details(maceration, fermentation, clarification and aging) [75, 76]. *Carménère* grape's pomace has high concentrations of anthocyanins, flavanols and flavonols

(Fig. **11**) [77]. Consequently, this biomass is a reach source to produce bioactive extracts.

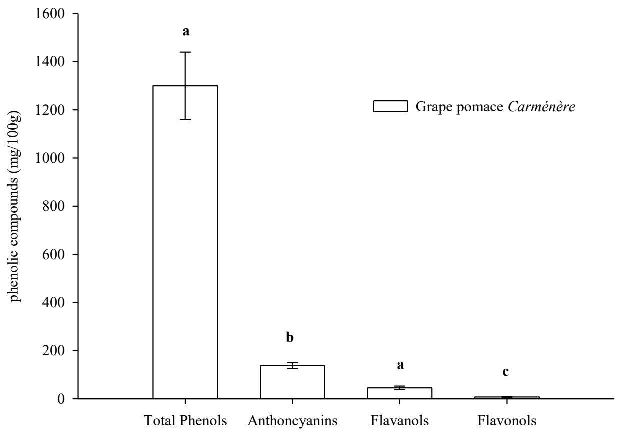

Fig. (11). Content of phenolic compounds present in *Carménère* grape pomace. a: expressed as gallic acid equivalent, b: expressed as malvidin equivalent, c: expressed as quercetin equivalent [77].

The demand for polyphenols has grown significantly in the recent years [1]. The price of these compounds varies with the degree of purity. For example, the price of epigallocatechin, quercetin and malvidin with 95% purity is $ 30,000, $ 30 and $ 7 per gram respectively [78]. In addition, the prices of concentrated extracts of polyphenols with concentrations between 20 and 40%, range between $ 50 and $ 75 per kilogram [79].

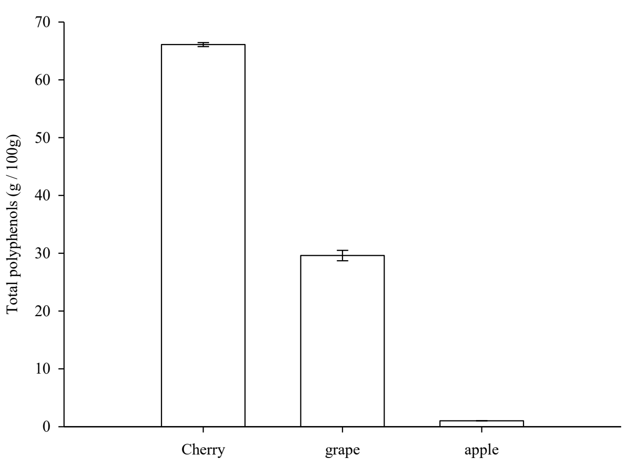

Fig. (12). Total polyphenol content in agro-industrial biomass [83-85].

Extracting these polyphenols from an agroindustrial biomass such as grape pomace can be performed through conventional techniques using organic solvents (solid-liquid extraction). These techniques however, are characterized by long processing times and the consumption of high amounts of solvents. Moreover, solvent recovery, extract safety and environmental impact are growing concerns. Furthermore, this type of extraction causes oxidation and hydrolysis of polyphenols [80, 81]. Hot pressurized liquid extraction (HPLE) is an alternative technique that overcomes many of the limitations of conventional extraction. In this method, the liquid solvent (normally pure water or hydroalcoholic mixtures) is subjected to pressures between 10 and 15 MPa and temperatures between 50 and 200°C [81]. Under these conditions, the solvent remains in the liquid state, enhancing the extraction of polyphenolic compounds [81, 82].

There are several agro-industrial natural sources for producing polyphenol extracts (Fig. **12**), although their polyphenol content varies depending on the type of processing to which the biomass has been subjected. Hence, the recovery of polyphenols from *Carménère* grape pomace is an economically attractive option considering the high price of polyphenol extracts, the high concentration of polyphenols in the grape pomace after wine fermentation and the application of alternative extraction technologies.

CONCLUSION

Carménère is the emblematic grape of Chile; it presents a particular polyphenolic profile with significant concentrations of malvidin, quercetin, myricetin and epigallocatechin. These compounds are responsible for the characteristics that distinguish its wines from other commercial wines. The polyphenols identified in *Carménère* have bioactive properties in the treatment and prevention of diseases associated with oxidative stress. Given the particularity of the *Carménère* polyphenols' profile, research regarding extraction, concentration and purification of their polyphenols should be encouraged. Obtained extracts could be used to produce functional foods, nutraceuticals and enological additives to moderate wine astringency and stabilize color in aged wines.

CONFLICT OF INTEREST

The authors declare that there are not conflicts of interest in this review.

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