

REVIEW

***Arbutus unedo* L. and its benefits on human health**

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Summary

Arbutus unedo has been long used in folk medicine, throughout Mediterranean countries, with the employment of infusions and decoctions of almost all parts of this plant: leaves, fruits, barks and roots. The application of these traditional remedies arises from several health-promoting characteristics, for treatment of gastrointestinal and urological problems, hypertension and cardiac diseases, diabetes and as anti-inflammatory agent, among other interesting properties. Antioxidant ability of *A. unedo* shrub is also known, and antimicrobial activity has also been reported. Several compounds present in different parts of the plant may be linked to these properties. Included in those are carotenoids, flavonoids, phenolic acids and vitamins (C and E). Other bioactive compounds may be also found in different parts of *A. unedo*, like terpenoids and organic acids. This review will focus on the known composition of several parts of *A. unedo*, their antioxidant ability and traditional use, and the available data sustaining the rationality of the use as part of folk medicine.

Keywords

Arbutus unedo; chemical composition; biological properties; folk medicine

In the recent years there has been an increased interest in natural products, leading to an extensive search for bioactive compounds, namely plant antioxidants, and their significance in medicine, food industry and human nutrition [1].

Arbutus unedo L., the strawberry-tree, belongs to the family of *Ericaceae* and is an ever-green shrub (Fig. 1A), native in the Mediterranean region. In Europe, it grows mostly in the Mediterranean basin (Portugal, Spain, France, Italy, Albania, Greece, Bosnia and Herzegovina, Croatia, Macedonia, Montenegro, Serbia and Slovenia) including some Mediterranean islands (Balearic, Corsica, Sardinia, Sicily and Crete), mainly in coastal and inland areas where climate is adequate to its development [2]. It has also been able to adapt to conditions of the south-western coast of Ireland [2] (Fig. 2). Although occasionally reaching a height of 12m, it is normally between 1.5m to 3m tall [3]. The fruits are conspicuous, globular, orange-red when ripe, growing up to 2cm in diameter (Fig. 1B, 1C). The flower is a clump of little cream-coloured lanterns. The maturation

phase of the fruits usually comprises two periods. The first starts in the middle of October and ends in the beginning of December, while the second happens around New Year's Eve [4]. The leaves are alternate, simple, with oblanceolate form and a dark green colour, leathery, short-stalked and toothed [5]. There are several qualities associated with this plant, such as ornamental, ecological and economical value, as well as therapeutic and medicinal properties. It is a popular ornamental tree, producing red fruits and pinkish-white flowers, which appear during winter months and increase the value for planting and ornamental purposes [5]. This plant also has an important role from the ecological point of view. It helps to maintain the diversity of the fauna, avoids erosion of the soils, it regenerates rapidly after fires, grows in poor soils [6] and it may be used for phytoremediation, namely against arsenic contamination [7]. The fruits, even though edible, are usually consumed as jams, marmalades or distilled into liquors [4]. Strawberry-tree honey is popular for its strong and distinctly bitter taste and has also been subject

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Fig. 1. *Arbutus unedo*.

A – tree, B – unripe fruits, C – ripe fruits.



Fig. 2. Approximate distribution of *Arbutus unedo* L.

Tab.1. Traditional medicinal uses of different parts of *A. unedo* plant.

Part used	Medicinal use	Reference
Leaves	Gastrointestinal disorders, urological problems, dermatologic problems, cardio-vascular application, kidney diseases, hypertension, cardiac diseases, diabetes, antihemorrhoidal, diuretic, anti-inflammatory, anti-diarrheal	12, 14, 15, 16, 49
Fruits	Gastrointestinal disorders, urological problems, dermatologic problems, kidney diseases, cardio-vascular application	12, 14, 15
Bark	Gastrointestinal disorders, urological problems, dermatologic problems, cardio-vascular application	16
Roots	Gastrointestinal disorders, urological problems, dermatologic problems, cardio-vascular application, hypertension, cardiac diseases, diabetes, diuretic, anti-inflammatory, anti-diarrheal	17, 18, 19, 49

to some studies [8, 9]. Organic acid composition, its total contents of phenolic compounds, as well as its physicochemical and melissopalynological properties are known [8]. The production of jams, liquors and honey based on *A. unedo* represent an economic importance of this shrub in rural areas [10]. There are several reports on the use of different parts of this plant in traditional medicine (Tab. 1). The plant contains a wide variety of antioxidant compounds (Fig. 3). Fruits are used in folk medicine as antiseptic, diuretic and laxative agents [11–15]. Leaves of this shrub are used as an infusion for their astringent, diuretic, urinary anti-septic, antidiarrheal and depurative agents. More recently they are used in the therapy of hypertension, diabetes, and in the treatment of inflammatory diseases [11, 16–18]. Other parts of this plant, such as roots and bark, are also used in traditional medicine, in the treatment of gastrointestinal disorders, as well as at urological and dermatologic problems [15, 19] using decoction of the roots as

a method to prepare the “drug”. Besides all this facts, this tree still keeps on being underexploited, mainly due to the high heterogeneity of the plants. All these described medicinal and therapeutical characteristics are linked to the contents of several biologically active compounds in different parts of *A. unedo*. This review will focus on the composition of different parts of the *A. unedo* shrub, as well as on the known biological activity and health-promoting effects of extracts of this plant.

LEAVES

Chemical composition

In the leaves of *A. unedo*, different phytochemical compounds are present, such as terpenoids, α -tocopherol, essential oils and phenolic compounds. The most important phenolics are presented in Fig. 4. The known terpenoids found in the leaves are α -amyrin acetate, betulinic acid and

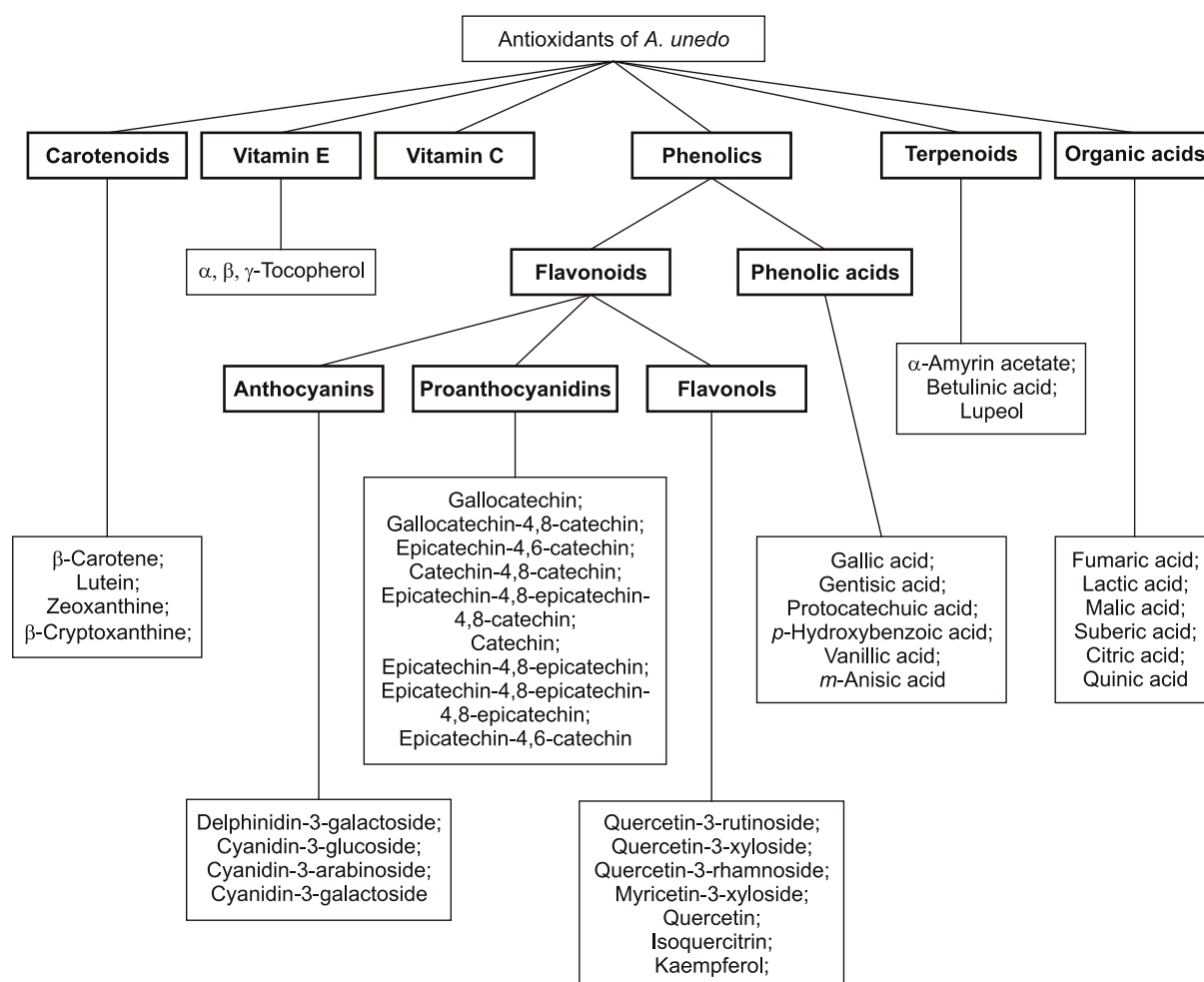


Fig. 3. Antioxidant compounds present in the *Arbutus unedo* tree.

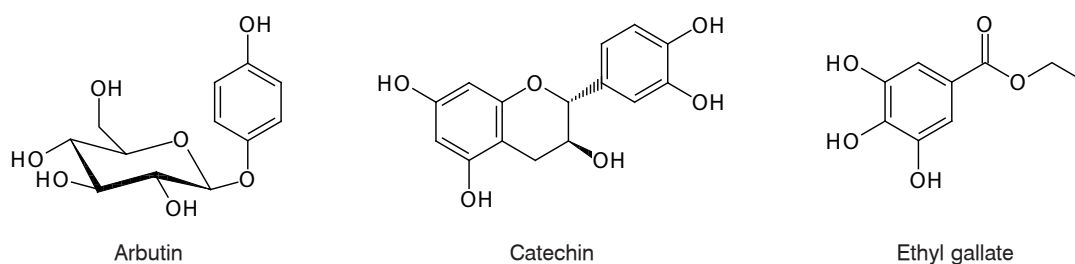


Fig. 4. Chemical structures of the most abundant phenolic compounds in *A. unedo* leaves.

lupeol [20]. The α -tocopherol amount present varies, depending on the time of collection of the samples. The highest amount is found when the leaves are collected in March, reaching the content of 132.8 mg of α -tocopherol per kilogram of dry weight. Although this appears to be a very low amount, it is very similar to the quantity present in the major industrial source of α -tocopherol, the soya bean [21]. The composition of the essential oil of *A. unedo* has already been determined by KIVCAK et al. [22], with major components identified as (*E*)-2-decenal, α -terpineol, hexadecanoic acid and (*E*)-2-undecenal. The phenolic fraction of the leaves includes a large variety of compounds: tannins, flavonoids (catechin gallate, myricetin, rutin, afzelin, juglanin, avicularin), phenolic glycosides (quercitrin, isoquercitrin, hyperoside) and iridoid glucosides [5, 23–25]. Polyphenols have been identified and quantified by FIORENTINO et al. [26]. This work allowed the identification of twelve compounds (arbutin, ethyl gallate, *p*-hydroxybenzoyl arbutin, galloyl arbutin, galocatechin, catechin, kaempferol 3-*O*- α -L-ramnopyranoside, quercetin 3-*O*- α -L-ramnopyranoside, myricetin 3-*O*- α -L-ramnopyranoside, kaempferol 3-*O*- β -D-arabinofuranoside, quercetin 3-*O*- β -D-arabinofuranoside and myricetin 3-*O*- β -D-arabinofuranoside). The major polyphenolic compound was found to be arbutin (627 mg·kg⁻¹ of fresh leaves), followed by catechin (546 mg·kg⁻¹ of fresh leaves) and ethyl gallate (440 mg·kg⁻¹ of fresh leaves). The amount of phenolic compounds present in the leaves, quantified using the Folin–Ciocalteu's phenol reagent, and performed in extracts obtained using different solvents, achieved as much as 192.66 mg of gallic acid equivalents (GAE) per gram of extract [27].

Antioxidant ability

Although the leaves contain a wide variety of antioxidant compounds, the information available on the antioxidant ability of the leaves is scarce.

An initial study was performed by PABUÇCUOĞLU et al. [28], and a more comprehensive study was performed by OLIVEIRA et al. [27]. In the former study, the authors studied the antioxidant activity of ethanolic and methanolic extracts of the leaves, using 2,2'-azino-bis(3-ethylbenzthiazoline-6-sulphonic acid) (ABTS^{•+}), and related the activity to the flavonol glycosides and tannins present in the leaves [28]. In the latter study, OLIVEIRA et al. [27] studied the antioxidant activity using three different methods (reducing power assay, scavenging effect on 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals and scavenging effect on superoxide radicals), and also quantified the total phenolics of the leaves [27]. Ethanolic extracts were found to be of the highest reducing power (extract concentration providing 0.5 of absorbance EC_{50} of 232.7 μ g·ml⁻¹) and the highest DPPH scavenging effect (EC_{50} of 63.2 μ g·ml⁻¹). In the scavenging assay on superoxide radical, methanolic extracts produced the best results (EC_{50} of 6.9 μ g·ml⁻¹). The amount of total phenols was as much as (192.66 \pm 1.66) mg GAE per gram of extract, when the leaves were extracted with ethanol [27]. The results demonstrated that the leaves of *A. unedo* possess a high scavenging effect against DPPH radical and a high reducing power, as well as a potent effect in scavenging superoxide radical, one of the most important free radical, the precursor of several molecules associated with tissue damage through oxidation [29].

FRUITS

Chemical composition

Fruits of *A. unedo* have also been subjected to some studies regarding their chemical composition [30, 31] (Tab. 2). Besides moisture, the most important component of the fruits, representing more than 50% of the total weight of the fresh fruit, are saccharides (938.3 g·kg⁻¹ \pm 4.1 g·kg⁻¹ of

dry weight). Proteins are also present in considerable amount, (33.6 ± 1.2) g [30] or (30.9 ± 0.8) g per kilogram of dry weight [31].

BARROS et al. [31] and OLIVEIRA et al [32] studied the fatty acid composition of *A. unedo* fruits. The first authors indicated the presence of twenty-one fatty acids [31], while OLIVEIRA et al. [32], identified and quantified 15 fatty acids. In both works, α -linolenic acid (C18:3n3) was found in higher amounts (36.51 ± 0.64 relative percent [31], ranging from 36.90 ± 1.75 relative percent in unripe fruits to 43.07 ± 0.16 relative percent in ripe fruits [32]). Polyunsaturated fatty acids represented the majority of all fatty acids (58.28 ± 0.54 relative percent [31] and 52.47 ± 4.26 relative percent in unripe fruits [32], 62.01 ± 0.26 relative percent in ripe fruits [32]).

Saccharides, minerals, phenolic compounds, organic and phenolic acids, vitamins and carotenoids are also present in the *A. unedo* berries. The amount of saccharides present in these fruits is variable between ripeness stages, being, $140 \text{ g} \cdot \text{kg}^{-1}$ of dry weight when unripe [10], and varying between $405.5 \text{ g} \cdot \text{kg}^{-1}$ to $522.1 \text{ g} \cdot \text{kg}^{-1}$ of dry weight when ripe [10, 33]. From total saccharides, when the fruit is unripe, saccharose is the major saccharide ($87.7 \text{ g} \cdot \text{kg}^{-1} \pm 0.6 \text{ g} \cdot \text{kg}^{-1}$ of dry fruit). When the fruits turn ripe, fructose becomes the most abundant saccharide present ($208 \text{ g} \cdot \text{kg}^{-1} \pm 2 \text{ g} \cdot \text{kg}^{-1}$ of dry fruit) [10].

Data on the mineral content of these fruits, determined by ÖZCAN and HACISEFEROĞULLARI [30], showed that they are a very good source of some minerals, in particular potassium (K), calcium (Ca), and phosphorus (P). Potassium is present in the berry of *A. unedo* in very high amounts, $(14909.08 \pm 1687) \text{ mg} \cdot \text{kg}^{-1}$ of dry weight, while calcium and phosphorus quantities are $(4959.02 \pm 15) \text{ mg} \cdot \text{kg}^{-1}$ and $(3668.56 \pm 339.69) \text{ mg} \cdot \text{kg}^{-1}$ of dry weight, respectively.

There are several organic and phenolic acids present in the *A. unedo* fruits. The organic acids

identified are fumaric ($1.94 \text{ g} \cdot \text{kg}^{-1}$ of dry weight), lactic ($0.84 \text{ g} \cdot \text{kg}^{-1}$ of dry weight), malic ($0.84 \text{ g} \cdot \text{kg}^{-1}$ of dry weight), suberic ($0.23 \text{ g} \cdot \text{kg}^{-1}$ of dry weight) and citric acids ($0.01 \text{ g} \cdot \text{kg}^{-1}$ of dry weight). [33]. Quinic acid is referred to by ALARCÃO-E-SILVA et al. [10] as the most important, both in unripe ($73.5 \text{ g} \cdot \text{kg}^{-1} \pm 0.3 \text{ g} \cdot \text{kg}^{-1}$ of dry weight) and ripe fruits ($59.9 \text{ g} \cdot \text{kg}^{-1} \pm 0.5 \text{ g} \cdot \text{kg}^{-1}$ of dry weight). In contrast to these data, AYAZ et al. [33] found fumaric acid as the major organic acid ($1.94 \text{ g} \cdot \text{kg}^{-1} \pm 0.7 \text{ g} \cdot \text{kg}^{-1}$ of dry weight) present in the ripe *A. unedo* fruits. Gallic ($10.7 \text{ g} \cdot \text{kg}^{-1}$ of dry weight), gentisic ($1.9 \text{ g} \cdot \text{kg}^{-1}$), protocatechuic ($0.6 \text{ g} \cdot \text{kg}^{-1}$), *p*-hydroxybenzoic ($0.3 \text{ g} \cdot \text{kg}^{-1}$), vanillic ($0.12 \text{ g} \cdot \text{kg}^{-1}$) and *m*-anisic ($0.05 \text{ g} \cdot \text{kg}^{-1}$) acids are the phenolic acids identified in these fruits [33].

The contents of vitamins and carotenoids in the fruits, although not being very high, should not be ignored. Data on the total vitamin E content was determined by BARROS et al. [31] and OLIVEIRA et al [32] showed that the fruits present in their composition (234.6 ± 2.6) $\text{mg} \cdot \text{kg}^{-1}$ of fruits' dry weight of total tocopherols [31] or (1368.58 ± 147.82) $\text{mg} \cdot \text{kg}^{-1}$ of oil extracted from unripe fruits. The most important form of vitamin E in the unripe fruits was found to be either α -tocopherol ($219.8 \text{ mg} \cdot \text{kg}^{-1} \pm 1.8 \text{ mg} \cdot \text{kg}^{-1}$ of dry weight [31]) or γ -tocotrienol ($1013.88 \text{ mg} \cdot \text{kg}^{-1} \pm 90.33 \text{ mg} \cdot \text{kg}^{-1}$ of oil [32]). The isomer α -tocopherol was also quantified in another work [13], where the amount of this form of vitamin E was found to be $(0.237 \pm 0.01) \text{ mg} \cdot \text{kg}^{-1}$ of edible portion. The quantities reported by those authors are quite dissimilar, and the different methodology used must account for such differences.

Another vitamin, vitamin C, has already been found in the berries of the strawberry tree. There are three known works that provide quantitative data on this vitamin. The highest amount was found by ALARCÃO-E-SILVA et al. [10], whose samples contained $(5420 \pm 110) \text{ mg}$ of ascorbic acid per kilogram of dry weight of the fruit, while BARROS et al. [31] found a lower value of only

Tab. 2. Chemical composition of *Arbutus unedo* fruits.

	ÖZCAN and HACISEFEROĞULLARI [30]	BARROS et al.* [31]
Moisture [$\text{g} \cdot \text{kg}^{-1}$]	537.2 ± 21.0	597.0 ± 26.7
Saccharides [$\text{g} \cdot \text{kg}^{-1}$]	–	938.3 ± 4.1
Proteins [$\text{g} \cdot \text{kg}^{-1}$]	33.6 ± 1.2	30.9 ± 0.8
Lipids [$\text{g} \cdot \text{kg}^{-1}$]	21 ± 1.0	13.7 ± 4.0
Ash [$\text{g} \cdot \text{kg}^{-1}$]	28.2 ± 1.24	17.1 ± 0.9
Energy [kJ]	13682 ± 544	16735.6 ± 48.9

(–) – not reported; * – expressed per kilogram of dry weight.

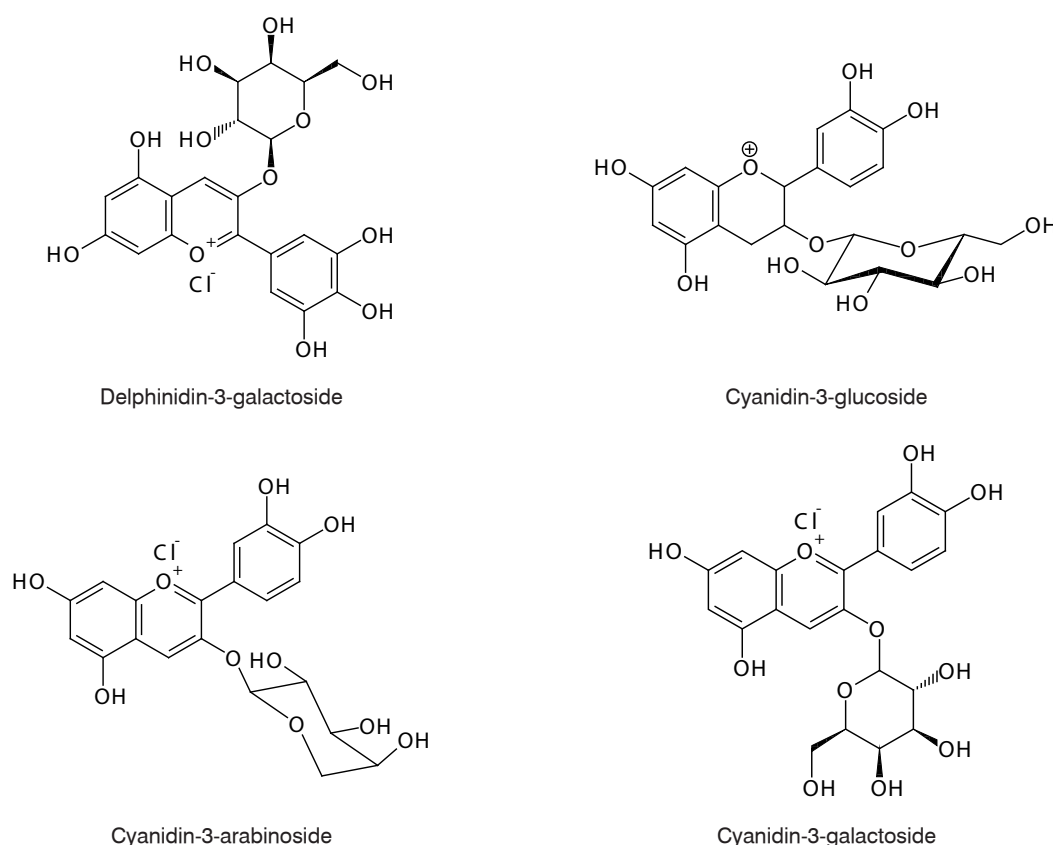


Fig. 5. Chemical structures of the anthocyanins present in *A. unedo* fruits.

(150.7 ± 7.7) mg of ascorbic acid per kilogram of dry weight. PALLAUF et al. [13] provided data on the content of vitamin C present in 100 g of edible portion of the strawberry-tree fruits. The quantity found by those authors, (55.0 ± 1.47) mg·kg⁻¹ of edible portion, although considered low, was comparable to the quantity present in other fruits, like peaches, apples or plums.

Carotenoids are also present in the fruits, in particular β -carotene. Total carotenoids were quantified by PALLAUF et al. [13], who reported contents of these compounds of (0.647 ± 0.14) mg·kg⁻¹ of edible portion, the major part being quantified as lutein plus zeaxanthine (0.427 mg·kg⁻¹ \pm 0.09 mg·kg⁻¹ of edible portion) and the remaining as β -carotene (0.25 mg·kg⁻¹ \pm 0.07 mg·kg⁻¹ of edible portion). The content of this carotenoid in this fruits was also determined by BARROS et al. [31] and ALARCÃO-E-SILVA et al. [10]. The former authors determined the value of (10.7 ± 0.9) mg·kg⁻¹ of dry weight as the amount of β -carotene that is present in the strawberry-tree fruits. ALARCÃO-E-SILVA et al. [10] indicated the changes in the amount of β -carotene with fruit ripening, beginning with

(381 ± 37) mg·kg⁻¹ of dry weight when the fruit is unripe, to (709 ± 52) mg·kg⁻¹ of dry weight when the fruit is red mature.

The phenolic fraction present in the fruits of this shrub includes several chemical classes, such as tannins, flavonoids, ellagic acid derivatives and gallic acid derivatives. The total phenolics were quantified in different studies: BARROS et al. [31] determined the value of (126.83 ± 66.6) g GAE per kilogram of extract, OLIVEIRA et al. [32] determined a maximum content when the fruits were in an intermediate stage of maturation, of (48.26 ± 4.49) g GAE per kilogram of extract. HEINRICH [34] reported a value of 37.6 g·kg⁻¹ of extract. In addition, FORTALEZAS et al. [35] reported a value of (16.46 ± 36.6) g GAE per kilogram of dry weight and ALARCÃO-E-SILVA et al. [10] reported a value of (15.5 ± 6) g catechin equivalents per kilogram of dry weight as the amount of total phenolics present in the fruits.

In the flavonoid class of compounds present in the berries, four different anthocyanins can be found: delphinidin-3-galactoside, cyanidin-3-glucoside, cyanidin-3-arabinoside [35, 36, 13] and cyanidin-3-galactoside (Fig. 5). The last compound

was found only by PALLAUF et al. [13], who were able to achieve the separation of two anthocyanin isomers that differ only in the saccharide present in the anthocyanidin, in this case the glucoside and galactoside of cyanidin, that may co-elute, interfering with both the identification and quantification of this kind of compounds [13]. Therefore, the statement of PAWLOWSKA et al. [36], who declare cyanidin-3-glucoside as the major anthocyanin present in these fruits (at $3.9 \text{ mg} \cdot \text{kg}^{-1}$ of fresh fruit) may not be entirely correct. PALLAUF et al. [13] claim that cyanidin-3-galactoside, the other isomer of this anthocyanin, is the major one, present in the berries at $(28.4 \pm 9.35) \text{ mg} \cdot \text{kg}^{-1}$ of edible portion, while the glucoside isomer is present in a very much lower amount ($1.2 \text{ mg} \cdot \text{kg}^{-1} \pm 0.25 \text{ mg} \cdot \text{kg}^{-1}$ of edible portion). The amount of these compounds was accessed by ALARCÃO-E-SILVA et al. [10], who quantified the total anthocyanin content of *A. unedo* fruits in two stages of maturation. The quantity of anthocyanins was found to increase during maturation, from $(0.25 \pm 0.2) \text{ g} \cdot \text{kg}^{-1}$ of dry weight when the fruit is unripe to $(1.01 \pm 0.1) \text{ g} \cdot \text{kg}^{-1}$ of dry weight as the fruit becomes red mature. In another study, FORTALEZAS et al. [35] quantified the total amount of anthocyanin, which reached the value of $(762.6 \pm 98.5) \text{ mg}$ of cyanidin 3-glucoside equivalents per kilogram of dry weight.

The content of tannins, present in fruits with different maturation stages, was studied by ALARCÃO-E-SILVA et al. [10]. According to those results,

the amount of tannins decreased as the fruit became ripe, from $(3.13 \pm 0.06) \text{ g} \cdot \text{kg}^{-1}$ of dry weight when the fruit was unripe to $(1.75 \pm 0.02) \text{ g} \cdot \text{kg}^{-1}$ of dry weight when the fruit was red mature. As the taste of the berries is considered to be too astringent when the fruits are green, becoming edible when they reach the ripening stage, this bitter taste can be attributed to the high content of tannins present, which are known to be astringent.

Another chemical group within flavonoids, the proanthocyanidins, are present in the fruits. Ten compounds were identified and quantified by PALLAUF et al. [13] including galocatechin, galocatechin-4,8-catechin, epicatechin-4,6-catechin, catechin-4,8-catechin, epicatechin-4,8-epicatechin-4,8-catechin, catechin, epicatechin-4,8-epicatechin, epicatechin-4,8-epicatechin-4,8-epicatechin and epicatechin-4,6-catechin. The total quantity of proanthocyanidins was found to be $(274.6 \pm 9.89) \text{ mg} \cdot \text{kg}^{-1}$ of edible portion, with epicatechin-4,8-epicatechin-4,8-catechin ($45.2 \text{ mg} \cdot \text{kg}^{-1} \pm 8.74 \text{ mg} \cdot \text{kg}^{-1}$ of edible portion) being the compound that most contributed to the large presence of proanthocyanidins in the fruits, followed by catechin and galocatechin (Fig. 6). Furthermore, among fruits, the strawberry-tree berries belong to those with high contents of these compounds [37].

Belonging also to flavonoids, flavonols are present as well. The most abundant are quercetin derivatives (quercetin-3-rutinoside, quercetin-3-xyloside and quercetin-3-rhamnoside), and myri-

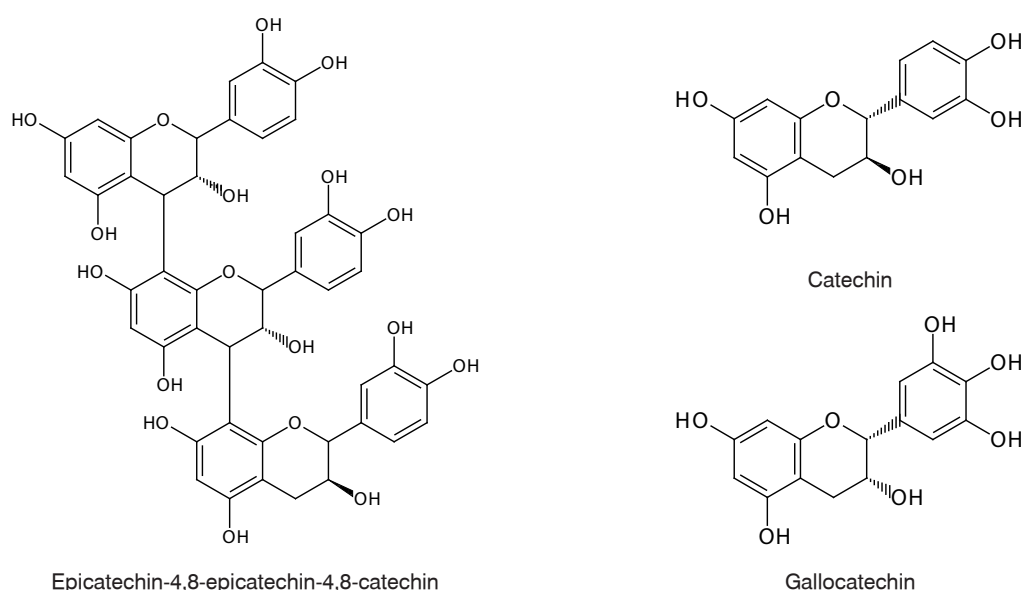


Fig. 6. Chemical structures of the most abundant proanthocyanidins present in *A. unedo* fruits.

cetin-3-xyloside is the fourth flavonol identified and quantified by PALLAUF et al. [13]. Other reports refer on the presence of quercetin, isoquercitrin and kaempferol [5, 38]. The total content of flavonols was found to be $(11.4 \pm 3.46) \text{ mg}\cdot\text{kg}^{-1}$ of edible portion, which amounts almost a half of the quantity of quercetin-3-xyloside ($5.2 \text{ mg}\cdot\text{kg}^{-1} \pm 0.31 \text{ mg}\cdot\text{kg}^{-1}$ of edible portion) [13].

Other antioxidant compounds present in *A. unedo* are ellagic acid and gallic acid derivatives. The former are present in amounts similar to flavanols ($15.4 \text{ mg}\cdot\text{kg}^{-1} \pm 1.62 \text{ mg}\cdot\text{kg}^{-1}$ of edible portion), with five derivatives having been found by PALLAUF et al. [13], namely, ellagic acid glucoside, ellagic acid diglucoside, methylellagic acid rhamnoside plus ellagic acid arabinoside and ellagic acid xyloside, which is the ellagic acid glucoside present in a higher amount ($4.6 \text{ mg}\cdot\text{kg}^{-1} \pm 0.19 \text{ mg}\cdot\text{kg}^{-1}$ of edible portion). Six derivatives of gallic acid were found in the strawberry-tree fruits (β -D-glucogalline, 3-O-galloylquinic acid, gallic acid 4-O- β -D-glucopyranoside, 5-O-galloylquinic acid, 5-O-galloylshikimic acid and 3-O-galloylshikimic acid).

Composition of volatiles has also been investigated in *A. unedo* berries. Besides studies on traditional distillate produced by fermentation of strawberry-tree fruits [4], strawberry-tree honey [39, 40], essential oils [41] and the emission of volatile organic compounds by the entire shrub [42–44], one report is available on the volatiles emitted by the berries themselves [45]. Six chemical classes were found (alcohols, aldehydes, esters, norisoprenoids, sesquiterpenes and monoterpenes), comprising 41 volatile compounds. Alcohols were found to be the main components of the volatile fraction of *A. unedo* fruits, followed by aldehydes and esters. The variations in volatiles was studied at three maturation stages of the fruits, and results show that the contents of all chemical classes decreased during ripening, with the exception of sesquiterpenes and monoterpenes. These appeared in higher amounts in ripe fruits than in unripe fruits. The major compounds were *cis*-3-hexen-1-ol, 1-hexanol, hexanal, *trans*-2-hexenal and acetic acid hexyl ester. A decrease in the contents of the compounds responsible for the characteristic green odours (alcohols, aldehydes and esters) was found to be paralleled by an increase in the contents of compounds associated with flower and sweet scents (mainly monoterpenes and norisoprenoids), present in ripe fruits of *A. unedo*.

Antioxidant ability

There are only three studies regarding the antioxidant activity of the fruits of *A. unedo*. The most

comprehensive one was performed by BARROS et al. [31], which used four different methods to evaluate such capacity: reducing power, scavenging activity on DPPH radicals, inhibition of β -carotene bleaching and inhibition of lipid peroxidation in brain tissue (TBARS). Low EC_{50} values (extract concentration providing 0.5 of absorbance, for the reducing power assay; extract concentration providing 50% antioxidant activity, in the remaining three methods) were determined for all the tested methods, ($447.92 \mu\text{g}\cdot\text{ml}^{-1} \pm 0.81 \mu\text{g}\cdot\text{ml}^{-1}$, $410.80 \mu\text{g}\cdot\text{ml}^{-1} \pm 0.93 \mu\text{g}\cdot\text{ml}^{-1}$, $774.99 \mu\text{g}\cdot\text{ml}^{-1} \pm 0.86 \mu\text{g}\cdot\text{ml}^{-1}$ and $94.27 \mu\text{g}\cdot\text{ml}^{-1} \pm 1.21 \mu\text{g}\cdot\text{ml}^{-1}$, respectively). The value determined by the TBARS inhibition method is particularly low. HEINRICH [34] tested several antioxidant and enzyme inhibition properties when studying 127 consumed wild or semi-wild plants that includes *A. unedo* fruits. Fruits presented high antioxidant activity on the DPPH assay (over 50% of the control) and medium protective ability against hydrogen peroxide-induced DNA damage (from 25% to 50% of the control). In the enzyme inhibition tests, high activity ($> 75\%$ of control) was determined in G-OH assay (protective ability against hydrogen peroxide-induced DNA damage) and medium activity in the test of xanthine oxidase. The third report on the antioxidant ability of strawberry-tree fruits, by FORTALEZAS et al. [35], presents the results on the antioxidant activity determined using the oxygen radical absorbance capacity (ORAC) method. The results showed a slightly lower activity ($11.66 \text{ mmol} \pm 2.01 \text{ mmol}$ Trolox equivalents per 100g of dry weight) than raspberry extracts ($15.37 \text{ mmol} \pm 2.73 \text{ mmol}$ Trolox equivalents per 100g of dry weight), used in that study as a control sample.

The entire shrub has also been subject to a study regarding its antioxidant ability. ANDRADE et al. [46] quantified the total phenolic content (grams of GAE per kilogram of plant extract) and flavonoid content (grams of quercetin equivalents per kilogram of plant extract), as well as the ability to scavenge DPPH radical, testing two different extraction methods (ethanol and acetone). The results showed a high amount of both phenolics ($255.19 \text{ g}\cdot\text{kg}^{-1} \pm 7.12 \text{ g}\cdot\text{kg}^{-1}$, in the ethanolic extract and $334.46 \text{ g}\cdot\text{kg}^{-1} \pm 31.83 \text{ g}\cdot\text{kg}^{-1}$ for the acetone extract) and flavonoids ($20.50 \text{ g}\cdot\text{kg}^{-1} \pm 0.77 \text{ g}\cdot\text{kg}^{-1}$, in the ethanolic extract and $23.37 \text{ g}\cdot\text{kg}^{-1} \pm 0.67 \text{ g}\cdot\text{kg}^{-1}$ for the acetone extract). The EC_{50} values of the extracts were considerably low, especially the one achieved with the ethanolic extraction ($7.85 \mu\text{g}\cdot\text{ml}^{-1}$), proving the high antioxidant ability of this shrub.

EFFECTS ON HUMAN HEALTH

Leaves

Leaves are traditionally used against some diseases, as mentioned before. There are several potential benefits to human health of *A. unedo* leaves, such as antioxidant activity, as described before, vasorelaxant effects, improvement of cardiovascular health, treatment or prevention of inflammatory diseases, and others. Some reports are available about specific effects of extracts of these leaves, which prove the rationality of the folk medicine. These works studied especially the vasorelaxant and anti-inflammatory properties of the extracts of the leaves. One example is the test of the extracts of *A. unedo* leaves using different solvents, to evaluate the vasorelaxant effect on Male Wistar rats' aortic ring [24]. The authors proved that leaves possessed a strong vasorelaxant activity, and this activity was mainly due to the presence of oligomeric condensed tannins and catechin galate. The effect of leaves on cardiovascular and inflammatory diseases was also studied, indicating that the extracts were able to decrease the platelet hyperaggregability, which is an important factor in the pathogenesis of inflammatory diseases [24].

MEKHFI et al. [47] showed that extracts of *A. unedo* leaves were able to inhibit in vitro thrombin-induced platelet aggregation, this activity being probably related with the presence of tannins in the leaves. This was further confirmed and the action of the extracts was found to be mainly due to the attenuation of the mobilization of Ca^{2+} ions, decrease in the reactive oxygen species production and protein tyrosine phosphorylation, proving that extracts of this leaves may be used to treat or prevent inflammatory and cardiovascular diseases [48].

MARIOTTO et al. [17] also proved the anti-inflammatory effects of leaves from strawberry tree. Their results showed that the leaves were able to down-regulate one of the initial factors of the inflammatory process on inflamed lungs of mice, member of transcription factors, signal transducers and activators of transcription family (STAT), and leading to a decrease in all parameters associated with inflammation, therefore proving to be a promising source of compounds able to reduce lung inflammation.

Furthermore, there is one report on the antimicrobial activity of extracts of the leaves of *A. unedo*. KIVCAK et al. [49] tested ethanolic extracts against Gram-positive, Gram-negative (*Escherichia coli*, *Staphylococcus aureus*, *S. epidermidis*, *Salmonella Typhimurium*, *Enterobacter cloacae* and *Enterococcus faecalis*), as well as against yeasts (*Candida al-*

bicans). The tested extracts proved to possess ability to inhibit the growth of all the tested bacteria.

Fruits

Several health-promoting properties have been attributed to *A. unedo* fruits, and exploited in folk medicine. However, as far as we know, only one study dealt with these attributes. HEINRICH [34] studied different parameters of the extracts of the fruits, performing enzyme inhibition tests (inhibition of xanthine oxidase, inhibition of myeloperoxidase-catalysed guaiacol oxidation, inhibition of acetylcholine esterase), inhibition of cytokine-induced cell activation (including the potential cytotoxicity of the extracts), assays measuring the anti-proliferation and anti-diabetic activity, and one assay investigating the effect on mood disorder-related biochemical parameters. In all the assays carried out, the fruits presented low activities in the anti-diabetic, mood disorder-related and anti-inflammatory assays. However, in the test of the anti-proliferative effect of the ethanolic extracts of the fruits, they showed a moderate activity, when compared to the control, proving to possess some ability to inhibit DNA synthesis and cellular proliferation. Furthermore, some reports are available about the traditional uses of the berries, for different diseases in several Mediterranean regions like Italy, Morocco and Turkey. That includes the use of fruits in the treatment of gastrointestinal disorders, dermatologic and urological problems and for cardio-vascular application [15], the ability of raw fruits to reduce kidney diseases [12] and against gastritis [14].

Other parts of this plant are also used in folk medicine. The roots are used for the treatment of several illnesses, which include abdominal pain, renal antispasmodic, bladder ailments, as an antihypercholesterolaemic or as a blood depurative [19] and for the treatment of diabetes, hypertension and cardiac disease [50], as diuretic, astringent, anti-inflammatory and antidiarrheal against blennorrhagia [16]. Furthermore, LEONTI et al. [15] reported that *A. unedo* bark was used for the treatment of gastrointestinal disorders, dermatologic and urological problems and for cardio-vascular application.

Different studies reported on the traditional use of the roots in the treatment of hypertension. ZIYYAT et al. [11] and AFKIR et al. [18] presented results proving the vasodilatory effect of the extract of roots, on rats, regressing the development of hypertension. Furthermore, MEKHFI et al. [51] proved the anti-aggregant properties of decocted roots, supporting the preventive and/or therapeutic properties linked to cardiovascular diseases

and decreasing the risk of thrombosis.

In another study, CARCACHE-BLANCO et al. [25] reported that a compound present and isolated from the entire plant caused inhibition of carcinogenesis, using two different methods (JB6 murine epidermal cell line assay and inhibition of the cyclooxygenase-2 (COX-2) enzyme), assays that represent major mechanisms of protection against tumour promotion.

Mechanisms of action of the antioxidants

There are three major mechanisms believed to be the way through which the antioxidants play protective role against oxidation agents: H-atom transfer, single electron transfer and metal chelation.

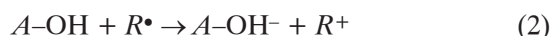
The first mechanism involves the transfer of a hydrogen atom to the free radical (Eq. 1).



where A is antioxidant and R is free radical.

Therefore, this free-radical becomes harmless, while the antioxidant, although becoming itself oxidized, it is also undamaging.

The second mechanism is called single electron transfer (Eq. 2).



It implies the donation of an electron from the antioxidant agent to the free radical. The free-radical anion is energetically stable with an even number of electrons, while the cation radical A^+ is also a less reactive radical species.

The third mechanism, known as Transition Metals Chelation, is explained by the possibility that antioxidant may chelate transition metal, leading to the formation of stable complexed compounds (Eq. 3).



where M^n is the transition metal.

This chelation prevents the metals from taking part in the reactions that may lead to the formation of free-radical, many of them considered the most dangerous ones.

The antioxidant activity of flavonoids, and therefore, of a large part of the antioxidants present in *A. unedo*, have been related to both their reducing ability, as well as to their metal-chelating properties [52].

On the other hand, carotenoids are able to scavenge free radicals by two different mechanisms: the above-mentioned electron transfer, and by another mechanism, known as the radical addition process, where the carotenoid molecule incorporates the free-radical in its structure [53].

Phenolics acids are able to act as antioxidants by two of the three described mechanisms: H-atom transfer and single electron transfer. However, it appears that these compounds are more active as antioxidants when using the first mechanism [54].

The vitamins present in *A. unedo* are reducing agents that counteract free radicals using the three mechanisms described above [55]. Together they form one of the most efficient synergistic interactions among antioxidants. This interaction is in particular important against lipid peroxidation of low-density lipoproteins (LDL), plasma and whole blood in vitro. As vitamin E is oxidized by a free radical, the subsequent vitamin E radical formed may be implicated in the initiation of another chain-oxidation process by attacking polyunsaturated lipids. If vitamin C is present, it reduces vitamin E radical to vitamin E, prior to lipid oxidation caused by the vitamin E radical. Moreover, it has been proven that the simultaneous presence of the two vitamins can completely inhibit the oxidation of LDL and plasma lipids [56].

The mechanism of action of the organic acids against antioxidants is believed to be the inhibition of the radical reaction in the oxidation processes [57].

As *A. unedo* contains a large number of different antioxidants, it could be that extracts of this plant may exert their antioxidant activity through one or more of the mechanisms.

CONCLUSION

Almost all parts of the *A. unedo* plant are used in traditional medicine, in a variety of forms and in several countries. Results obtained in studies with extracts of several parts of the plant, both in animal and human cells, support this traditional use, namely in the treatment of hypertension, cardiovascular diseases and diabetes. Those results open new possibilities for the use of this shrub, especially for the development of new drugs to treat the mentioned illnesses, as well as in the food industry, due to their antioxidant ability. The beneficial effects associated with this tree are linked to the contents of polyphenolic compounds. Further studies are needed to evaluate possible interactions between the intake of *A. unedo* and of other dietary constituents, the necessary dose of *A. unedo* ingestion that proves to be beneficial to humans, as well as to assess the bioavailability of the health-promoting compounds in humans. The in vivo antioxidant capacity as well as the safety of such compounds should be examined.

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