horticulturae

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Review

Strawberry Tree Fruits and Leaves (*Arbutus unedo* L.) as Raw Material for Sustainable Functional Food Processing: A Review

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Citation: Bebek Markovinović, A.; Brčić Karačonji, I.; Jurica, K.; Lasić, D.; Skendrović Babojelić, M.; Duralija, B.; Šic Žlabur, J.; Putnik, P.; Bursać Kovačević, D. Strawberry Tree Fruits and Leaves (*Arbutus unedo* L.) as Raw Material for Sustainable Functional Food Processing: A Review. *Horticulturae* **2022**, *8*, 881. https://doi.org/10.3390/horticulturae8100881

Academic Editor: Bastien Christ

Received: 25 August 2022
Accepted: 22 September 2022
Published: 26 September 2022

Abstract: The strawberry tree (*Arbutus unedo* L.) is a Mediterranean plant known for the traditional use of its fruits and leaves due to their health benefits. Thus, it has been used for years in folk medicine to relieve various health conditions such as urological and kidney problems, dermatological, cardiovascular and gastrointestinal diseases. The fruits are traditionally used for making jams, jellies, and strong alcoholic beverages, while the leaves are mostly used for preparing tea. Since the leaves were more researched, previous results indicated that they have important biological effects, so further research should focus on the fruits. Due to its chemical composition, rich polyphenolic profile and the biological potential derived from it, the plant has great prospects for the production of functional foods and nutraceuticals. However, the plant's potential is underutilized in terms of processing. Therefore, this review summarizes the properties and the potential of the fruits and leaves of *A. unedo* and their possible benefits for processing with respect to agricultural, nutritive, biological and economic values.

Keywords: *Arbutus unedo* L.; agriculture; biological potential; nutritive value; bioactive compounds

1. Introduction

The fruits of the strawberry tree (*Arbutus unedo* L.) are noticeable, globular, green, and orange to red in color (Figure 1). The fruits ripen several times during the year, in late September/mid-October to early December. The leaves of the strawberry tree are simple, alternately arranged, with serrated margins, leathery, dark green in color, and short-stalked. Since the flowering of the strawberry tree takes 12 months to flourish, the tree sometimes bears the ripe fruit and white-pink flowers at the same time, which creates a beautiful decorative atmosphere in the environment during the winter months [1]. Carl Linnaeus described and named the strawberry tree in volume one of his seminal 1753 work "Species Plantarum" with the Latin name *Arbutus unedo*, which is still used today [2]. The strawberry tree (*Arbutus unedo* L.) has long been used by people in the Mediterranean region mainly as fresh food or processed in various products, as medicine or as wood fuel for heating and cooking [3]. The strawberry tree belongs to the Ericaceae family and forms specific arbutoid mycorrhizae with some fungi [4]. This plant has been studied not only for its nutrient-rich fruits, but also for its biological properties. All parts of *A. unedo* have roles in Mediterranean folk medicine due to the high content of polyphenols and other phytochemicals [5].

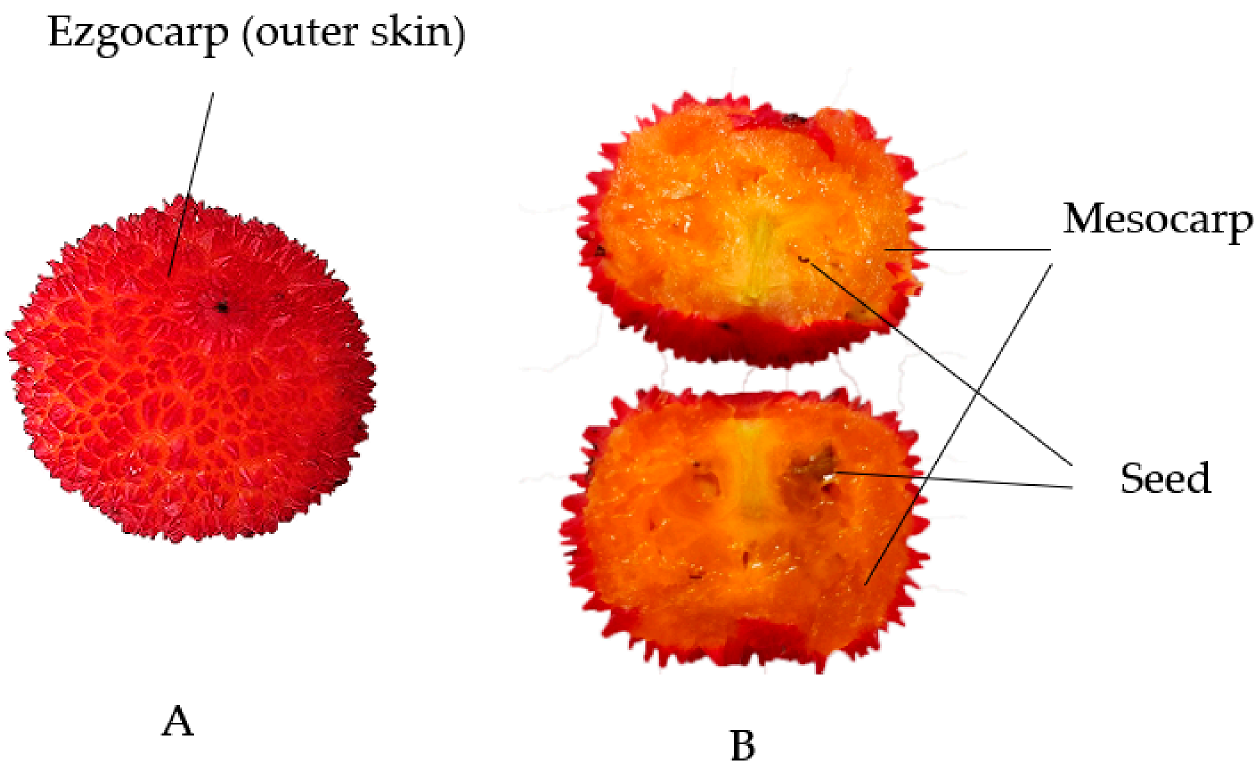

Figure 1. Strawberry tree (*Arbutus unedo* L.) fruit: (**A**) the whole fruit, and (**B**) cross section.

These phytochemicals have been studied for numerous biological activities, including antimicrobial, antioxidant, anti-inflammatory, anti-proliferative and anti-diabetic effects [5,6]. Additionally, polyphenols have the possibility to stimulate cellular defense and the enzymatic systems responsible for detoxification [1]. Strawberry tree leaf extracts have remarkable uroantiseptic, diuretic, astringent and antidiabetic properties [6–9]. The fruits of the strawberry tree play a role in folk medicine in the treatment of gastrointestinal, urological, cardiovascular and dermatological problems, due to their diuretic, antiseptic and laxative properties [5,9]. Decocts of the bark and roots of the strawberry tree are used in folk medicine for gastrointestinal, urological, cardiovascular and dermatological problems [10]. Strawberry tree root is used to relieve abdominal pain, lower cholesterol, treat bladder and kidney diseases, diabetes (by inhibiting glucose absorption in the intestine), treat hypertension and heart disease [10]. It is also used as a diuretic, anti-inflammatory and anti-diarrheal agent [10–12].

The most complete phenolic profile ("fingerprint") of strawberry tree leaves and fruits was recently established in Croatia. A strong correlation between total phenolic content and radical scavenging activity indicated that phenolic compounds are responsible for the antioxidant properties of *A. unedo* leaves and fruits [5].

The fruits of the strawberry tree are the most commonly consumed in the form of jams, marmalades or alcoholic distillates [10]. The honey of *A. unedo*, also known as "bitter honey," has a strong and astringent taste and a very high content of phenols [13]. The production of jams, marmalades or liqueurs from *A. unedo* fruit is often an important additional source of income, especially in rural areas, and its production confirms the economic potential of this shrubby tree.

Recently, consumers have been asking for foods that have a positive impact on their health, such as functional foods [14]. Since the strawberry tree is a nutritionally valuable food with strong biological potential that could be used to produce new products with positive effects on human health, this article aims to provide an overview of the agricultural, nutritional and biological potential of the fruits and leaves of the strawberry tree, and their possible processing for the production of functional foods.

2. Agriculture Perspective of Strawberry Tree Cultivation

Geographic Distribution of A. unedo L.

The fruits of the strawberry tree are traditionally used for human consumption in Mediterranean regions. The strawberry tree is an evergreen fruit species of the Ericaceae family with natural populations in: the Atlantic region of western Europe (including Ireland); European countries around the Mediterranean Sea; northeastern Africa (including Egypt and Libya); and the Canary Islands and western Asia (Figure 2), where frost is not very frequent and dry summer air is not very intense [15].

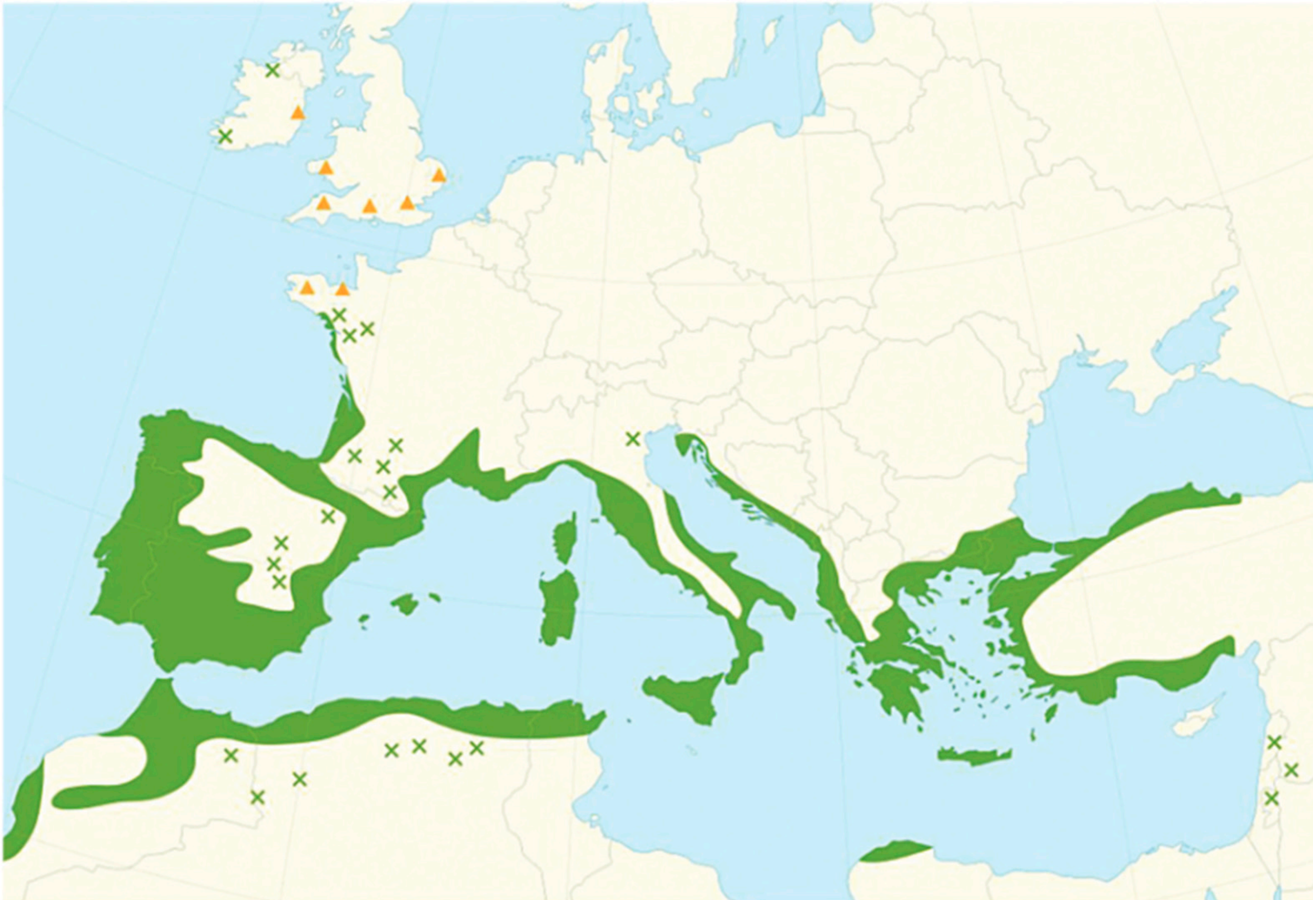

Figure 2. Geographic distribution of *Arbutus unedo* L. (source: Caudullo et al. [16], according to Skendrović Babojelić et al. [17]). Legend: natural habitat; × isolated populations; ▲ introduced and naturalized populations.

In Croatia, it is widely distributed as a natural wild plant along the Adriatic coast, from Istria to Dalmatia and the islands (Figure 3), and is an important component of the maquis vegetation and forests *Quercus ilex* L. [18].

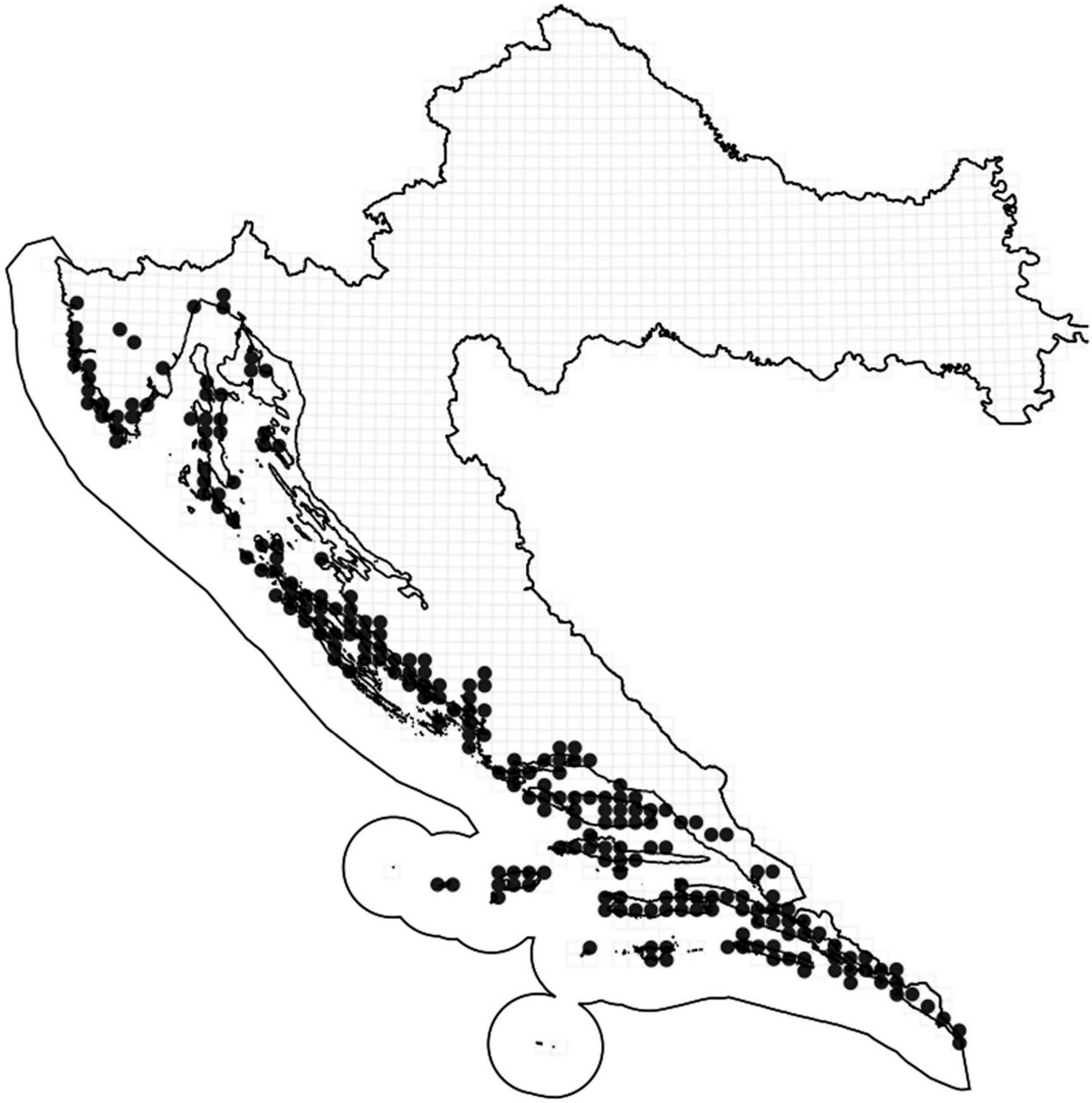

Figure 3. Distribution of wild plants of *Arbutus unedo* L. in Croatia according to the Flora Croatica Database [19].

In some countries, interest in strawberry trees is increasing and new selection studies are focusing on selecting highly productive cultivars with larger fruits. In Turkey, strawberry tree fruits have developed from a small local production to a niche product that fetches considerable prices [20].

In the last century, the cultivation of the strawberry tree has not yet been able to gain acceptance due to the lack of cultivars for higher production and better fruit quality, as well as quality information for cultivation techniques on a larger scale. According to Celikel et al. [21], selection was mainly done in China with the cultivars 'Zaose' [22], 'Dongkui' [23], 'Daliziyangme', 'Baiyangmei', 'Zaohongmei' and 'Dahuamei' [24]. On the market, there are several cultivars such as: 'Compacta', a smaller shrub, from 1.8 to 3 m tall and wide; 'Elfin King', which has a bordered, dwarf form, and flowers and fruits throughout the year; and 'Rubra' has deep pink flowers [25], which are mainly planted in backyards for ornamental purposes.

Some countries have implemented selection programs aimed at selecting strawberry tree genotypes with high fruit quality, promoting extensive cultivation, and preventing deforestation and excessive harvesting [21]. Given the growing interest of farmers, the selected cultivars need to be multiplied on a large scale using appropriate propagation techniques [3]. In Portugal, adult plants were selected and micro propagated to optimize fruit production and quality. It has been shown that it is possible to produce promising genotypes on a large scale and distribute them to farmers interested in this crop [26]. Nowadays, there are some plantations in Portugal and some research is being conducted [27]. In Italy (Sardinia), the fruits of 20 different genotypes have been characterized [28]. Additionally, in Turkey, the phenological and pomological characteristics of different genotypes of the common strawberry tree and species of Greek strawberry tree have been determined [29–32] according to Celikel et al. [21]. Strawberry trees are characterized by high genetic, morphological and phenological variability [15].

As with some other fruits, the quality of strawberry tree fruit is probably subject to various influences, such as: location; selection of plant material; growing conditions; cultivation techniques; and fruit ripening stage, etc. [33,34].

In areas where the average temperature in January is above 4 °C, growth and fertility are limited, and temperatures of −10 °C and below can cause plant death, which largely depends on the duration of low temperatures [17]. It is important to choose areas for growing strawberry trees that are not exposed to frequent occurrence of stress factors such as frost, hail, strong winds and prolonged drought. Naturally, strawberry trees grow in different soils, the pH of which ranges from 5.0 to 7.2. In addition to soil pH, soil texture and organic matter content must also be considered to get a better estimate. It is quite adaptable to different conditions and soil types [15,25]. The microsite is determined by longitude, altitude, slope, solar radiation, air and water drainage, species diversity and other factors. The strawberry tree usually grows between 20 m and 1000 m above sea level [35], but it can grow up to 1200 m high [36]. It grows best and bears fruit when the entire plant is in full or partial sun [15,25]. The reproductive cycle of strawberry trees is much longer than that of other fruit tree species; from flowering to fruit ripening it lasts the whole year, which should be taken into account.

In nature, the strawberry tree is propagated by seeds, which leads to a greater diversity of genetic and morphological characteristics of wild plants. For the establishment of a modern plantation, it is necessary to use plant material with high yield potential and high-quality fruit. Fertilization before planting is the most important basis for successful planting and obtaining a good yield and fruit quality, because the plants are perennial and remain in the same place for a long time [37]. The establishment of some first strawberry tree plantations shows that clonal plants had significantly higher fruit production when fertilized, while the lowest values were observed in seedlings without fertilization [27]. Row orientation (north-south preferred) and plant spacing in and between rows are also important.

To achieve excellent fruit quality, regular implementation of agro- and pomotechnical measures must be taken into account when growing strawberry trees [17]. Since the strawberry tree is a species that can have very lush vegetation under good growing conditions, several maintenance measures are required in strawberry tree cultivation to be successful: tree pruning and training system; irrigation; orchard maintenance; fertilization; pollination; pest, disease and weed control; and fruit harvesting, etc.

According to the International Center for Underutilized Crops and the Global Facilitation Unit for Underutilized Species [38], the strawberry tree belongs to the category of neglected or underutilized species. The strawberry tree belongs to a species that has been traditionally collected throughout the Mediterranean region since ancient times for its valuable medicinal and aromatic properties [26]. It is considered an underappreciated fruit species with various commercial uses, from the production of fresh fruit and processed products, to its use in the food, pharmaceutical and chemical industries, beekeeping, reforestation, as an ornamental plant and for other purposes. The strawberry tree has extraordinary ecological importance as it prevents soil erosion and regenerates quickly after fire [15]. It is also important for biodiversity as it forms different plant associations and provides shelter and food for various organisms such as insects, fungi, birds and mammals [17].

The introduction of these wild fruit species into cultivation could exploit their economic and environmental potential and contribute to the sustainability of horticultural production.

3. Nutritive Value of Strawberry Tree

3.1. Fruits

The components of the nutritional and chemical composition of strawberry tree fruits, through their content and mutual interactions, determine the sensory, nutritional and biological properties of the raw material, as well as the final product. The fruits contain a variety of compounds with excellent nutritional quality, including sugars, unsaturated fatty acids, organic and phenolic acids, fibers, vitamins, proteins and carotenoids [39]. Given the basic nutritional and chemical composition, strawberry tree fruits are characterized by a high sugar content, mainly fructose (20–30%), and glucose (about 20%), followed by sucrose (1.5–3%) and maltose (1–2%) [10]. The chemical composition of strawberry tree fruits depends on climatic conditions, soil and seasonal harvest [10]. Given the specific ripening stages of strawberry tree fruits (not all ripen at the same time), the carbohydrate contents vary greatly. For example, sucrose content may be even lower at the fully ripe stage due to hydrolysis on glucose and fructose during ripening. Because of the high carbohydrate content, the fruits of the strawberry tree also have a high energy value. However, care should be taken when eating them, as the slight fermentation of the fruit can cause digestive problems. In addition to sugar, the fruits are also rich in fiber, both soluble and insoluble, with pectin being the most abundant, which also distinguishes this species from a health point of view.

With regards to mineral composition, strawberry tree fruits are a very good source of potassium, calcium, phosphorus, magnesium and sodium [39,40]. In addition, the fruits are rich in vitamins, and the high content of vitamins C and E is particularly noteworthy. Some researchers indicate that fresh strawberry tree fruit may contain between 200 and 300 mg 100 g^{-1} fresh weight (FW) of vitamin C, while vitamin E in unripe fruit may be as high as 1369 mg kg^{-1} FW [34]. In a study conducted in Croatia, the highest vitamin C content was found in wild varieties with 402.41 mg 100 g^{-1} FW [37], which proves that this species can be considered a very good source of vitamin C, even several times higher than certain fruits and vegetables known for their high content of this vitamin, such as citrus fruits, kiwi, peppers, parsley and others. Moreover, fatty acids with a favorable ratio of $\omega3/\omega6$-fatty acids have been detected in the fruit, which is due to the linolenic acid, which accounts for 58% of the total percentage of fatty acids [10].

Strawberry tree fruits are also characterized by a high content of polyphenolic compounds, including phenolic acids, flavonoids, anthocyanins, catechuic tannins, gallic tannins, coumarins, quinones and anthraquinones, which makes them a plant material with an extremely high antioxidant potential [15,39]. The polyphenolic contents and polyphenolic profiles of strawberry tree fruits differ greatly in different studies, which is primarily a consequence of the specific environmental factors (e.g., climatic conditions) of the particular site where the fruits were collected. For example: El Cadi et al. [41] reported the total polyphenolic contents of fruits collected in northern Morocco ranged from 34.8 to 51.61 mg GAE g^{-1} dry weight (DW); Ruiz-Rodríguez et al. [42] as 9.51 to 19.73 mg GAE g^{-1} DW in fruits from Spain; Mendes et al. [43] found an average of 16.7 mg GAE g^{-1} DW in fruits collected in Portugal; Barros et al. [44] found an average value of 126.83 mg GAE g^{-1} DW in fruits from the northeastern regions of Portugal; while Colak [45] reported an average value of 557 mg GAE 100 g^{-1} FW from fruits collected in the eastern region of Turkey. Šic Žlabur et al. [37] studied strawberry tree fruits from different locations on the Croatian Adriatic coast (from northern parts to the southern parts, including the islands) and determined a total phenolic contents ranged from 14.29 (Hvar island) to 18.94 to 18.94 mg GAE g^{-1} DW (Cres island) [37], proving that not only the location but also the specific microsite has a strong influence on the content of polyphenolic compounds.

In addition to the total phenolic content, the fruits of the strawberry tree are also rich in flavonoids and anthocyanins, as shown by various studies. The total anthocyanin contents varied considerably depending on the analyst or location, but also on the ripening stage of the fruits, with the following values found: from 0.13 to 1.42 mg pelargonidin-3-glucoside g^{-1} DW [41], 762.6 mg cyanidin-3-glucoside kg^{-1} DW [46]; from 1.23 to 21.73 mg kg^{-1} FW [37]. Alarcão-e-Silva et al. [47] found that the total anthocyanin contents in strawberry tree fruits varied according to the ripening stage, with the total anthocyanin content increasing during ripening from 0.25 g kg^{-1} DW in unripe fruits to 1.01 g kg^{-1} DW in red fruits (fully ripe).

Among anthocyanins, delphinidin-3-galactoside, cyanidin-3-glucoside, cyanidin-3-arabinoside and cyanidin-3-galactoside were determined [46,48,49]. As described in the literature [48], the most abundant anthocyanin detected in strawberry tree fruits is cyanidin-3-glucoside (average 3.9 mg kg^{-1} FW), while other authors [49] have managed to distinguish two anthocyanin isomers differing only by the saccharide contained in anthocyanidin, in this case the glucoside and galactoside of cyanidin, and suggested that the most abundant anthocyanin is cyanidin-3-galactoside, with the other isomer containing an average of 28.4 mg kg^{-1} FW. Similar results were obtained in a study on fruits of wild variety from southern Italy (Pisa region). The most abundant anthocyanins were cyanidin-3-*O*-glucose, cyanidin-3-*O*-arabinoside and delphinidin-3-*O*-galactoside [48].

As mentioned earlier, it is important to emphasize that the polyphenolic profile of individual compounds varies greatly depending on the location and also on the stage of ripeness of the fruit [15]. Accordingly, El Cadi et al. [41] reported values for total flavonoid contents ranging from 37.43 to 41.51 mg quercetin g^{-1} DW, Barros et al. [44] reported an average value of 34.99 mg g^{-1} extract, while Šic Žlabur et al. [37] found values ranging from 7 to 15.58 mg catechin g^{-1} DW. Regarding the phenolic acids, quinic, protocatechuic, gallic, caffeic, ferulic, cinnamic, ellagic, syringic, hydroxycoumarin and vanillic acids were strongly represented [41,50,51]. Considering the flavones, dihydroxyflavone is the most abundant [41]; of the flavan-3-ols, catechins, epicatechins, procyanidin dimer with corresponding gallate and prodelphinidin; and of the flavonols, the hexoside of isorhamnetin, myricetin, quercetin, kaempferol and apigenin are the most abundant [41]. As suggested by some studies [50], the most abundant compound from the group of polyphenols detected in the fruits of strawberry tree collected in Turkey was gallic acid, followed by gentisic, protocatechuic, *p*-hydroxybenzoic, vanillic and *m*-anisic acids. Different authors from Spain [52] quantified the main important polyphenols (mg 100 g^{-1} DW) as follows: catechins (313.4); hydroxybenzoic acids (112.2); hydroxycinnamic acids (1.0); flavonols (3.6); ellagic acid (6.9); anthocyanins (5.8); and procyanidins (474.1).

Differences were also found in other polyphenols, for example, in flavonol content between fruits collected in Portugal and Spain. Myricetin-3-*O*-xyloside and quercetin-3-*O*-xyloside were not detected in fruits from Portugal, whereas this was the case in Spanish samples, while quercetin-3-*O*-rutinoside and quercetin-3-*O*-rhamnoside were present in both Portuguese and Spanish wild samples. Moreover, in wild fruits from northeastern Portugal, the main phenolic compounds were flavan-3-ols and galloyl derivatives (60.93 mg 100 g^{-1}), followed by anthocyanins (13.77 mg 100 g^{-1}) and flavonols (10.86 mg 100 g^{-1}) [53]. Within the group of flavan-3-ols and galloyl derivatives, in a study conducted in Spain Pallauf et al. indicated gallocatechin, gallocatechin-4,8-catechin, the proanthocyanidin dimers and epicatechin as the most abundant [49].

The identification of volatile compounds in the fruits of the strawberry tree led to the determination of 41 compounds, which are divided into several subclasses: alcohols are the most abundant volatile compounds; followed by aldehydes and esters. It should be noted that the contents of the listed compounds decrease sharply during ripening. Norisoprenoid derivatives, sesquiterpenes and monoterpenes are other volatile compounds found in strawberry tree fruit, but in very small amounts. The amount of these compounds also varies greatly with the progress of fruit ripening. The content of monoterpenes decreases from unripe to mid-ripe and is highest at the ripe stage. The content of sesquiterpenes increases from unripe to mid-ripeness, after which it is lower. The content of norisoprenoid derivatives decreases with ripeness, which also confirms the fact that the content of volatile compounds strongly depends on the ripening stage of strawberry tree fruit [51].

3.2. Leaves

In addition to the fruit, the leaf of the strawberry tree is also an important raw material for both nutritional and medicinal purposes. Strawberry tree leaves have a high dry matter content (51–92%), total acidity ranging from 0.7–1.9%, higher acidity, and pH ranging from 3.89 to 5.35, which depends on the location and climate [37]. They also contain various types of phytochemical compounds such as phenolic compounds, vitamins, terpenoids and essential oils [51]. In general, according to the numerous studies conducted, the leaves of the strawberry tree contain a significantly higher content of polyphenolic compounds than the fruits, so the leaf can be considered as a valuable material, especially in terms of human health. Oliveira et al. [54] determined the total phenolic content of strawberry tree leaf extract to average 192.66 mg GAE g^{-1}; Mendes et al. [43] reported values of total phenolic content in leaves to average 170.3 mg GAE g^{-1}; Bouyahya et al. [55] obtained results for total phenolic content ranging from 94.51 and 141.726 GAE mg g^{-1} extract depending on the solvent type; Šic Žlabur et al. [37] between 18.69 and 26.94 mg GAE g^{-1} FW; Martins et al. [56] reported values for total phenolic content between 254.96 and 495.24 mg g^{-1} leaf FW; and Brčić Karačonji et al. between 67.07 and 104.74 mg GAE g^{-1} DW [5].

Regarding polyphenols, here several compounds have been determined, such as: tannins; flavonoids (catechin gallate, myricetin, rutin, afzelin, juglanin, avicularin); phenolic glycosides (quercitrin, isoquercitrin, hyperoside); and iridoid glucosides [57–60], of which arbutin (62.7 mg 100 g^{-1} FW), ethyl gallate (44.00 mg 100 g^{-1} FW) and catechin (54.6 mg 100 g^{-1} FW) were the most abundant [61]. Hydroquinone, a bioactive metabolite of arbutin, was not detected in any leaf of *A. unedo* [62]. Thanks to advances in analytical techniques, the detailed profiles of leaf phenolics have been established in recent years. Using an ultra-high-performance liquid chromatograph (UHPLC) coupled with a hybrid mass spectrometer-(LTQ OrbiTrap MS), a total of 60 phenols have been identified in the aqueous and methanolic leaf extracts. Flavonoid aglycones (morin, naringenin, myricetin and kaempferol), phenolic acids (protocatechuic acid and chlorogenic acid), and arbutin and its derivatives were detected in leaves, but not in fruits [5]. Using the same technique, Maldini et al. [11] detected 19 phenols in ethanolic leaf extracts from Sardinia. The main phenols detected were flavonoids, mainly quercetin, kaempferol and myricetin derivatives. With a liquid chromatograph coupled with a quadrupole time-of-flight mass spectrometer (LC-QTOF-MS), a total of 37 phytochemicals were detected, and the main constituents in the leaf extracts being phenolic acids, iridoids, proanthocyanidins and flavonoids [8]. The levels of total flavonoids (expressed as % of quercetin) measured in the leaves ranged from 0.52 to 2.14% [7]. In addition, Jurica et al. [7] determined for the first time the total phenolic acid content in the leaf extracts and it was 1.48%, expressed as % of rosemarinic acid.

When observing terpenoids, amyrin acetate, betulinic acid and lupeol were strongly represented in the leaves [44]. Among vitamins, α-tocopherol and vitamin C stand out as highly contained. Further, authors from Croatia determined that the vitamin C contents in the leaves of wild strawberry trees collected from different locations on the Adriatic coast ranged from 61.61 to even 333.83 mg 100 g^{-1} FW [37].

Among the macroelements in the leaves of *A. unedo*, potassium (1743 mg 100 g^{-1} DW) and calcium (1299 mg 100 g^{-1} DW) were the most abundant, while iron (26.8 mg 100 g^{-1} DW) was the most abundant of the microelements [63], which was similar to the mineral profile in the fruits. According to Asmaa et al. [63] the most abundant volatiles in *A. unedo* leaves were: camphor (43.5%); α-fenchone (17.5%); bornyl acetate (16.0%); eucarvone (3.16%); and myrtenyl acetate (3.16%). Kivack et al. [64] reported that (E)-2-decenal (12.0%); α-terpineol (8.8%); hexadecanoic acid (5.1%); and (E)-2-undecenal (4.8%) were the most abundant. These compositional differences may be the result of differences in cultivation area or extraction procedure [65]. Among the fatty acids, according to Koukos et al. [66], linolenic acid was the most abundant (44.2%), followed by palmitic acid (25.5%) and linoleic acid (7.9%), while according to Dib et al. [67], palmitic acid was the most abundant (38.5%), followed by oleic acid (10.6%), linolenic acid (9.3%) and linoleic fatty acid (5.5%).

Total carotenoid contents ranged from 0.06 to 0.27 mg g^{-1}, and chlorophyll concentrations from 0.19 to 2.37 mg g^{-1}, again which could be correlated with the climate and geolocation [37]. According to Kachoul et al. [68] the anthocyanin contents in strawberry tree leaves ranged from 0.33 to 0.8 mg of cyanidin-3-glucoside per gram of extract, depending on the type of solvent and the extraction procedure.

Since the fruits and leaves of the strawberry tree are a rich source of nutrients and bioactive compounds (Table 1) attributed with various biological activities, they represent a perspective raw material to be considered for the development and formulation of functional foods and nutraceuticals.

Table 1. Individual bioactive compounds found in *A. unedo* fruits and leaves.

Plant Source	Analytics	Bioactive Compound	Concentration	References
Fruit	HPLC	Gallic acid	4.56–36.93 mg 100 g^{-1} DW	[69]
		Protocatechuic	1.84–5.90 mg 100 g^{-1} DW	
		Gallocatechin	16.15–65.31 mg 100 g^{-1} DW	
		Catechin	22.09–49.36 mg 100 g^{-1} DW	
		Chlorogenic acid	5.55–27.42 mg 100 g^{-1} DW	
		Syringic acid	4.27–7.94 mg 100 g^{-1} DW	
		Ellagic acid	8.42–33.73 mg 100 g^{-1} DW	
		Quercetin-3-xyloside	1.43–4.09 mg 100 g^{-1} DW	
		Rutin	0.90–1.26 mg 100 g^{-1} DW	
		Quercetin-3-galactoside	1.66–3.46 mg 100 g^{-1} DW	
		Quercetin-3-glucoside	2.11–2.89 mg 100 g^{-1} DW	
		Cyanidin-3-glucoside	0.43–7.21 mg 100 g^{-1} DW	
		Cyanidin-3-arabinoside	0.36–1.64 mg 100 g^{-1} DW	
Fruit	HPLC-TQ-MS/MS	4-hydroxybenzoic acid	0.34–0.50 mg 100 g^{-1} DW	[70]
		Gallic acid	1.4–4.7 mg 100 g^{-1} DW	
		Syringic acid	0.63 mg 100 g^{-1} DW	
		Chlorogenic acid	0.676 mg 100 g^{-1} DW	
		Quercetin	0.79–0.84 mg 100 g^{-1} DW	
		Quercetin 3-β-glucoside	1.7–2.6 mg 100 g^{-1} DW	
		Rutin	0.43–0.57 mg 100 g^{-1} DW	
		Kaempherol	0.39–0.74 mg 100 g^{-1} DW	
		Catequin	28–149 mg 100 g^{-1} DW	
		Epigallocatechin	10–26 mg 100 g^{-1} DW	
		Naringin	0.35 mg 100 g^{-1} DW	
Fruit	MS/MS	Arbutin	NQ	[11]
		Myricetin pentoside	NQ	
		Myricetin rhamnoside	NQ	
		Kaempferol-rhamnoside (afzelin)	NQ	
Fruit	HPLC	Protocatechuic acid	0.11–0.61 mg 100 g^{-1} FW	[71]
		Vanillic acid	0.10–1.17 mg 100 g^{-1} FW	
		Ellagic acid	1.11–2.13 mg 100 g^{-1} FW	
		Rutin	0.15–0.95 mg 100 g^{-1} FW	
		Quercetin	0.12–0.31 mg 100 g^{-1} FW	
		Gallic acid	1.62–7.29 mg 100 g^{-1} FW	
		Catechin	1.16–5.75 mg 100 g^{-1} FW	
Leaves	UHPLC-LTQ Orbitrap MS	Gallocatechin	64.21–211.60 mg kg^{-1} DW	[5]

Table 1. *Cont.*

Plant Source	Analytics	Bioactive Compound	Concentration	References
		Protocatechuic acid	1.27–2.47 mg kg^{-1} DW	
		Aesculin	1.95–5.88 mg kg^{-1} DW	
		Chlorogenic acid	ND–1.95 mg kg^{-1} DW	
		Catechin	47.73–102.95 mg kg^{-1} DW	
		p-Hydroxybenzoic acid	16.21–27.08 mg kg^{-1} DW	
		Caffeic acid	2.61–5.75 mg kg^{-1} DW	
		Syringic acid	0.66–2.67 mg kg^{-1} DW	
		Vanillic acid	3.71–7.96 mg kg^{-1} DW	
		Rutin	29.93–106.03 mg kg^{-1} DW	
		p-Hydroxyphenylacetic acid	4.35–6.57 mg kg^{-1} DW	
		Hyperoside	635.10–1512.94 mg kg^{-1} DW	
		p-Coumaric acid	10.11–32.83 mg kg^{-1} DW	
		Catechin gallate	34.48–73.70 mg kg^{-1} DW	
		Ferulic acid	2.55–4.85 mg kg^{-1} DW	
		Myricetin	ND–1.78 mg kg^{-1} DW	
		Quercetin	41.28–124.91 mg kg^{-1} DW	
		Naringenin	ND–4.39 mg kg^{-1} DW	
		Kaempferol	10.63–35.50 mg kg^{-1} DW	
Leaves	HPTLC	Quercitrin	1.21–2.20 mg g^{-1} DW	[72]
		Isoquercitrin	ND–0.33 mg g^{-1} DW	
		Hyperoside	ND–0.35 mg g^{-1} DW	
		Chlorogenic acid	0.61–1.46 mg g^{-1} DW	
Leaves	HPLC-PDA	Chlorogenic acid	0.8–6.5 mg g^{-1} DW	[73]
		Caffeic acid	0.6–1.0 mg g^{-1} DW	
		p-Coumaric acid	0.2–6.6 mg g^{-1} DW	
		Quercetin	0.5–10.7 mg g^{-1} DW	
Leaves	GC-MS	Arbutin	2.75–6.82 mg g^{-1} DW	[74]
Leaves	HPLC-PDA	Arbutin	12.1 mg g^{-1} DW	[75]

UHPLC-LTQ Orbitrap MS—ultra-high performance liquid chromatography- linear ion trap-Orbitrap hybrid mass spectrometry; DW—Dry weight; FW—Fresh weight; ND—not detected; HPTLC—high-performance thin-layer chromatography; HPLC-PDA—high-performance liquid chromatography-photo diode array detection; GC-MS—gas chromatography-mass spectrometry.

4. Biological Potential of Strawberry Tree

Because polyphenols are potent antioxidants against oxidative stress caused by oxygenic metabolites, the total concentration of phenols is critical to understanding the health-promoting properties of these plants. The determination of total phenols, phenolic acids, tannins, flavonoids and vitamin E (tocopherols in seeds) as known antioxidants has been carried out in numerous studies [5,51,76].

The phytochemical profiling of fruits and leaves revealed the presence of flavonoids, iridoids, anthocyanins carotenoids, terpenoids and fatty acids as major classes of bioactive constituents [8]. However, based on the literature search, it seems that the leaves of the strawberry tree have been researched in much more extensive way than the fruits.

4.1. Fruits

Considering the favorable nutritional composition, especially the extremely high contents of numerous phytochemicals, particularly polyphenolic compounds, vitamins and dietary fibers, it is not surprising that the nutritional and medicinal values of these delightful fruits were known since ancient Greece and are used today. They are mainly used in Mediterranean countries, for traditional, industrial, chemical and pharmaceutical purposes [42]. The fruits of the plant are traditionally used as antiseptic, diuretic and laxative, carminative, digestive, odontalgic and cardiotonic [77–79]. Scientific studies suggested that strawberry tree fruits also have high pharmacological potential due to their in vitro and preclinical antibacterial, anti-inflammatory, antitumor and antioxidant properties [6,8]. For example, Salem et al. [80] studied the antimicrobial activity of ethanolic extract of strawberry tree fruits and concluded that they have strong antibacterial effects on *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Bacillus subtilis*, and a moderate effect on *Salmonella typhimurium*, *Enterococcus feacium*, *Escherichia coli* and *Candida albicans*. It should be noted that the antimicrobial effects were influenced by the choice of extraction solvents and the extraction procedures [81,82].

Since the fruits are rich in polyphenolic compounds (mainly phenolic acids, flavonoids and anthocyanins), vitamins (especially C and E) and other bioactive compounds, their antioxidant and free radical scavenging activity is very pronounced. Many literature data emphasized high antioxidant activity of strawberry tree fruits [15,37,83,84] which consider this species very important for the prevention of numerous diseases, especially neurodegenerative [46], cardiovascular [85] and diabetes/hypoglycemia [8], while some of the polyphenols identified in strawberry tree fruits have a strong anticancer effect [86]. Possibly, the anticancer effects tested on different tumor cell lines were likely related to the gallic acid derivatives that are dominant in the fruits [87].

Moreover, since fruits are rich in flavonoids, it is important to highlight that flavonoids are highly effective scavengers of most types of oxidizing molecules, including singlet oxygen and various free radicals, which may be involved in DNA damages and promotion of tumors [88]. The fruits can be successfully used in the treatment of various urological [89], dermatological [90] and gastrointestinal problems [91]. The anti-radical activities of strawberry fruits were investigated in the study by Mendes et al. [43], using experimental human cell line models. This was one of the first studies to evaluate the antioxidant activity of *A. unedo* on human biological membranes. In general, the results of the study suggested that both the fruits and leaves were promising sources of natural antioxidants that can be used in free radical-induced diseases. Figure 4 shows the biological and functional properties of *A. unedo* plant [6,12,55,58,68,83,85,86,92–94].

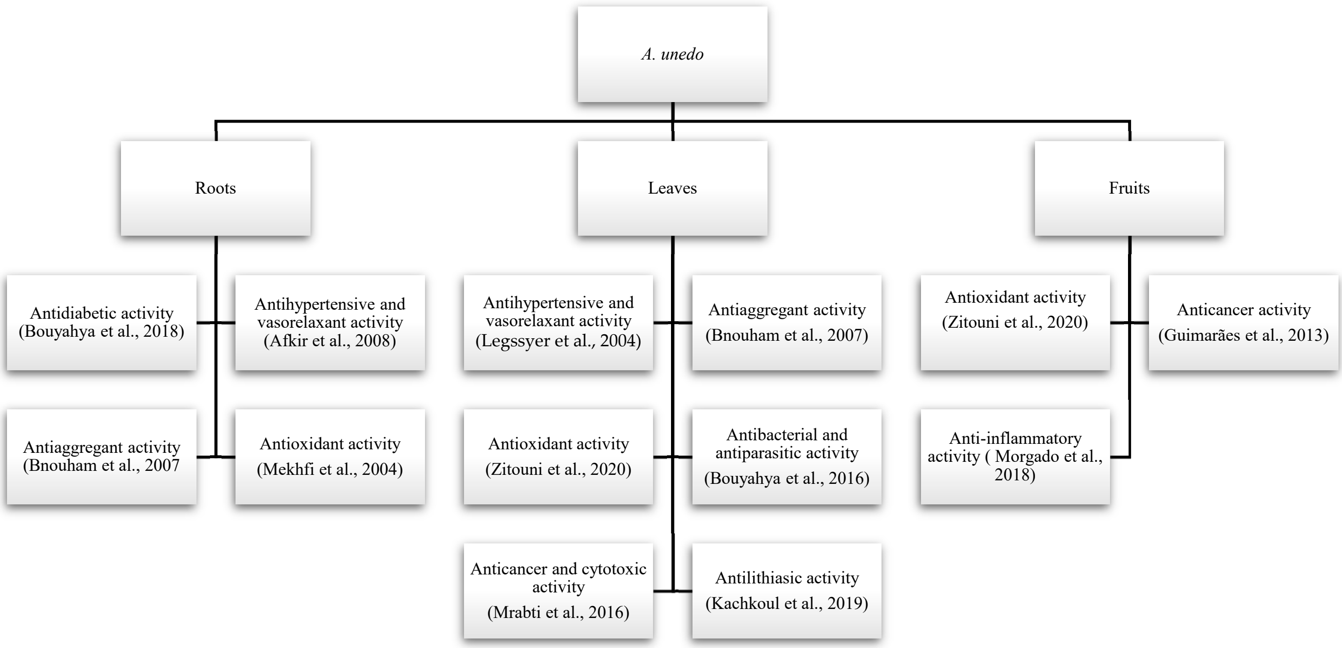

Figure 4. Biological and functional properties of *Arbutus unedo* L. plant [6,12,55,58,68,83,85,86,92–94].

4.2. Leaves

Since polyphenols are strong antioxidants that protect the organism from oxidative stress caused by reactive oxygen species, the determination of total phenols and groups of phenolic compounds (tannins, flavonoids and phenolic acids) as well as individual phenols, could lead to an understanding of the biological potential of *A. unedo* [1]. The wide range of values for total phenolic contents obtained in different studies was the result of differences in the climate in which *A. unedo* grows, as well as different extraction methods and the types of solvents used to extract the active compounds from the leaves [5,8,54,95].

Jurica et al. [7] reported that tannins accounted for 83% of the total phenols in the leaves. Therefore, the strong antioxidant activity of leaves can be attributed, among other things, to the higher content of tannins which have a strong antioxidant effect due to the large number of hydroxyl and galoyl groups.

The importance of flavonoids lies in the fact that some of them (e.g., the flavonols myricetin, rutin, quercetin and querictrin) have high free radical scavenging activities, and some (catechins) have the ability to chelate metals and thus prevent the formation of free radicals [96]. Phenolic acids show different radical scavenging activities depending on the number and the position of hydroxyl groups and methoxy substitutions in the molecules [96].

The antioxidant properties of *A. unedo* leaves were studied by different spectrophotometric methods. Ferric reducing antioxidant power (FRAP) method showed better activity of the methanolic extracts (1.896 mmol $FeSO_4$ g^{-1}) than the aqueous counterparts (1.187 mmol $FeSO_4$ g^{-1}). The 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid (ABTS) assay also favored the methanolic extracts (165.510 mg TE g^{-1}), as compared to the aqueous alternative (130.172 mg TE g^{-1}) [7]. The superiority of alcoholic over aqueous extraction of leaf phenolics was also reported in the study by Kachkoul et al. [68] who found that the hydroalcoholic extracts exerted higher antioxidant capacities than the aqueous extracts, using the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay (IC_{50} 76.14 μg mL^{-1} versus 202.64 μg mL^{-1} and the FRAP assay (53.77 μg mL^{-1} versus 236.86 μg mL^{-1}). Several studies have investigated the radical scavenging activity of *A. unedo* leaf samples by the DPPH method, indicating a large antiradical activity (IC_{50} 23–95 mg L^{-1}), more efficient phenolic extraction with methanol or ethanol than with water, and a strong correlation between the phenolic content and antioxidant activity [5,7,11]. In addition to the high content of the phenolic glycoside arbutin, the high antioxidant activity measured in the ABTS assay could be due to the high content of quinic acid, which belongs to the polyols, so there might be another class of compounds, hence different from phenolics, responsible for antioxidative activity of the leaves [62].

The extracts from the leaves were able to reduce platelet adhesion (coagulation), which is an important factor in the pathogenesis of inflammatory diseases. The treatment of human platelets with an increasing concentration of crude water leaf extracts (0.015–1.5 mg mL^{-1}) reduced thrombin-induced platelet aggregation in a concentration-dependent manner. This activity was probably related to the presence of tannins from leaves [97]. In an ex vivo study on isolated rat aorta, the extract from the leaves of *A. unedo* (0.01 g L^{-1}) showed potent vasodilatory properties and improvement in cardiovascular health that correlated with the presence of condensed tannins and catechin gallates [58]. This was additional to inhibition of enzymes related to rheumatoid arthritis, tumor cell proliferation, and metastases with the existence of gallic acid derivatives [98].

Arbutin showed antibacterial activities especially against *Enteroccocus* species [7,99]. The mechanism of action was the same as in bearberry leaves (*Arctostaphylos uva-ursi* L.), which contained higher amounts of arbutin than the strawberry tree. The antimicrobial effects of arbutin was strongly dependent on the extracellular activity of beta-glucosidase, an enzyme responsible for the conversion of arbutin to free hydroquinone, which was responsible for antimicrobial activity [7]. Leaf extracts also inhibited the growth of *Candida tropicalis*, and *Crataegus lucitaniae* [100], various mycobacteria and *Leishmania* parasites [39].

The extracts of fresh leaves obtained by ethanolic ultrasonic extraction (IC_{50} 19.56 mg L^{-1}) and hydroethanolic maceration (IC_{50} 19.56 mg L^{-1}) showed hypoglicemic activities by inhibiting beta-glucosidase, digestive enzyme responsible for carbohydrate absorption [8], while the leaf infusion showed litholytic activity against calcium oxalate stones in vitro [68].

The cytotoxic effects of the leaf extracts were tested on different tumor cell lines, whereas the cytoprotective effect were tested only on isolated human lymphocytes. The hydromethanolic leaf extract caused a blockade of the cell cycle G2/N phase in human osteosarcoma cells U2OS and did not induce apoptotic cell death, indicating cytostatic rather than cytotoxic effects. In contrast, cytotoxicity against human umbilical vein endothelial cells (HUVEC) was reported [9]. An extract of leaf protein of *A. unedo* showed an inhibitory effect on in HT29 colon cancer cells [101].

Jurica et al. [102] performed an in vitro safety assessment of 24 h exposure of lymphocyte to aqueous leaf extracts and reported absence of cytotoxic effects at a concentrations equivalent to the maximum allowable daily intake of arbutin, with negligible potential to cause primary DNA damages, while preventing micronuclei formations in lymphocytes.

As described above, the biological activities of leaves have been extensively investigated only in vitro, while there are only few important in vivo studies despite their well-documented health-promoting properties. Further, Jurica et al. [103–105] evaluated the in vivo safety of an aqueous leaf extracts administered *per os* to rats at a dose of 200 mg kg^{-1} body weight day^{-1} for 14 and 28 days. Following exposure to the extract, low DNA damages in white blood cells and no significant changes in the hematological parameters were observed [103]. The leaf extracts showed high biocompatibility with liver and kidney tissues by preserving organ function and DNA integrity in rat organ cells [105,106]. Table 2 shows a summary of some biological potentials of the fruits and leaves of the strawberry tree recently reported.

Table 2. Biological potential of *Arbutus unedo* L. fruits and leaves.

Part of Plant	Type of Study	Biological Potential	References
Leaves	Determination of growth inhibition zones by radial diffusion	Antibacterial and antifungal potential	[95]
Leaves	Determination of growth inhibition zones by disc diffusion	Antibacterial and antifungal potential	[106]
Fruits	Determination of MIC by dilution on broth media	Antibacterial potential	[107]
Leaves	In vitro platelet aggregation	Antiaggregant potential	[97]
Leaves	In vitro platelet aggregation	Antiaggregant potential	[108]
Fruits	In vitro, BrdU assay	Antitumoral potential	[84]
Fruits	DPPH assay, scavenging activity, β-carotene bleaching activity	Antioxidant potential	[109]
Leaves	DPPH assay	Antioxidant potential	[110]
Leaves and fruits	ORAC assay, MMP-9 inhibitory activity assay	Antioxidant potential	[98]
Leaves	FRAP, Lipid peroxidation, DPPH assay	Antioxidant potential	[75]
Fruits	DPPH assay, DNA damage	Antioxidant potential	[84]
Leaves	Inflammatory activation, In vitro inhibition of STAT1 activation	Anti-inflammatory potential	[111,112]

MIC—Minimal inhibitory concentration; BrdU—5-Bromo-2-deoxyuridine; DPPH—1,1-Diphenyl-2-picrylhydrazyl; ORAC—oxygen radical absorbance capacity; MMP-9—matrix metalloproteinase-9; FRAP—ferric reducing antioxidant power; STAT1—signal transducer and activator of transcription 1.

5. Economic Properties of Strawberry Tree

Aware of the fact that an insufficient, and unbalanced diet has negative impacts on their health, consumers have recently been demanding minimally processed products with preserved nutritional properties, preferably without any additives or only with natural origin. For the above reasons, there is a growing demand for functional foods that are expected to have a positive effect on consumers' health [113]. Due to various needs, lactose intolerance, allergies or simply the need for a healthier diet, consumers are increasingly turning to the consumption of plant products rich in bioactive ingredients. Plants, especially fruits, containing bioactive compounds with positive impacts on human health, including polyphenolic compounds and dietary fibers in particular. Therefore, the modern food industry needs new ingredients to enrich existing products. *A. unedo*, due to its chemical composition and contents of bioactive compounds that contribute to biological potential, can be considered an excellent ingredient for improving and enriching existing products or developing new functional products. Honey from *A. unedo* flowers, for example, is an expensive product with strong, unique and very special sensory properties. It has a characteristic coffee-like flavor, yellow-brown color and sweet-bitter taste characteristic of products containing arbutin [114]. Considering that arbutin was found in 83% of strawberry tree honey samples, it can be considered as a marker for *A. unedo* honey [115]. Due to its antioxidant, biological and antimicrobial properties, *A. unedo* honey can be used for cosmetic and pharmaceutical purposes in addition to its use in food manufacturing [115]. In the study conducted by Mrabti et al. [116], the root of *A. unedo* plant also showed antibacterial and antioxidant activities and therefore has the potential to be used in the production of functional foods and nutraceuticals. However, most of the products made from *A. unedo* were obtained from the fruits and leaves of the plant.

Currently, the development of new technologies and concepts in the context of Industry 4.0, such as 3D printing, opens up various opportunities for the use of fruit and leaf extracts in the production of functional foods and nutraceuticals with the aim of improving health [117]. *A. unedo* certainly has proven its potential, but it is anticipated that this plant will be increasingly used in processing as we strongly move toward sustainable food production.

5.1. Fruits

Because of its high pectin content, strawberry tree fruits are traditionally used to make jams, jellies and marmalades [118,119]. Furthermore, the fruits are traditionally used to produce an alcoholic beverage called "Koumaro" in Greece and "Aguardente de medronho" in Portugal [120]. In the production of spirits, fermentation is the most important step. Since strawberry tree fruit spirits are traditionally produced under uncontrolled conditions, there are significant differences in the alcohol and methanol contents of such beverages [120]. The formation of methanol is a consequence of the activity of specialized enzymes, methyl esterizes during the process of methyl esterification of pectin, which is naturally present in the fruits of *A. unedo* [121]. Methanol is a dangerous product for human health, and according to the European regulation for spirits, the maximum allowed concentration is 1000 g hL^{-1} of pure alcohol [122]. In most cases, the methanol concentration in this alcoholic beverage is below or close to the allowable limit, which depends on the ripeness of the fruit, fermentation conditions and distillation technology [123–126]. In this direction, Anjos et al. [127] created a new spirit by fermentation of strawberry tree fruits and honey with significantly lower contents of methanol and other harmful compounds than the commonly produced spirits of this plant. In order to reduce the variation in alcohol content and to produce a uniform product, Soufleros et al. [120] proposed the systematic production and standardization of the spirit manufacturing process, which opened the possibility for expanding and strengthening the economy of businesses that produce this alcoholic beverage.

As noted previously, fruit extracts have high antioxidant activity due to their high polyphenolic contents; Ganhao et al. [52] investigated the effects of adding *A. unedo* fruit extracts to raw pork burger patties by DPPH and ABTS methods, as well as with thiobarbituric acid reactive substances and color stability during 12 days of storage. They concluded that the extracts exhibited significant antioxidant activity against lipid oxidation and slowed down the color changes of meat caused by oxidation processes, making them suitable ingredients for the production of new meat-based functional products [52]. Similarly, Masmoudi et al. [128] investigated the influences of fruit extracts on antioxidant activity; studying the physicochemical, textural and sensory properties of "Sardaigne" cheese. The addition of the fruit extracts had no negative effects on the color and sensory properties of the product, while improving the firmness and increased the utilization and antioxidant activity of the product. Similar results in terms of antioxidant activity were found by Cossu et al. [129] who added strawberry tree fruit extract to yogurt. In conclusion, *A. unedo* fruit extracts represent potential for use as a functional ingredient in dairy [128,129] and meat products. Following on, Takwa et al. [130] added strawberry tree fruit extracts to bread and studied the antioxidant and antimicrobial properties. The results showed that the fruit extracts had preservative effects that also enriched the product with bioactive compounds.

Considering the above data, strawberry tree fruits and its extracts can be considered as functional ingredients that can improve existing foods or create new functional products in various fields of food industry.

5.2. Leaves

Due to their rich polyphenolic composition, *A. unedo* leaves are most commonly used for the extraction and enrichment of other products with polyphenolic compounds. To that end, Derbassi et al. [131] incorporated *A. unedo* leaf extracts into Quark cheese and studied their preservation effects for 8 days, together with antioxidant activity. Compared to commercially available additives (potassium sorbate), the extracts showed better antimicrobial properties. Moreover, the antioxidant activity remained strong even after the extracts were incorporated into the product. This confirms the possibility of using the extracts from the leaves of *A. unedo* as natural additives in the production of healthy, functional foods with improved biological properties.

In addition to the antioxidant activity, Dias et al. [132] also investigated the potential of leaf extracts as an anti-browning agent in fresh-cut pears. The results showed that the increased polyphenolic contents correlated with better effectiveness of enzymatic inhibition in the samples. Therefore, these results possibly suggested the application of leaf extracts as an anti-browning agent in fresh products and ultimately prolonging their shorter shelf life.

Erkekoglou et al. studied the contents of phenolic compounds in hot and cold nonalcoholic beverages prepared from these leaves [133]. The authors concluded that decoction is a more suitable method for the preparation of a phenol-rich beverage than infusion. Therefore, these data indicated great possibility for the use of strawberry tree leaves for the preparation of functional infusions and soft drinks.

In addition to the potential use of *A. unedo* leaves in the manufacturing of functional foods, they can also be important for pharmacological and medicinal purposes due to their polyphenolic composition. For instance, the high content of palmitic acid indicates that the leaves are a valuable industrial ingredient for the production of soaps and cosmetics [134]. Similarly, arbutin from leaves is light and pH stable, making it suitable for uses in cosmetics, while through the processes of hydrolysis and oxidation in the aqueous matrix, it can be transformed into benzoquinone, which has antibacterial properties [135,136]. For this reason, and due to the fact that arbutin is a good alternative to hydroquinone, it is suitable for the apical products for the treatment of hyperpigmentation [137]. Figure 5 summarizes the economic properties and further economic prospects of strawberry tree fruits and leaves. In conclusion, the leaves of strawberry tree, as well as the fruits, have great potential for the enrichment of existing or the creation of new functional products, and further research is needed in this area.

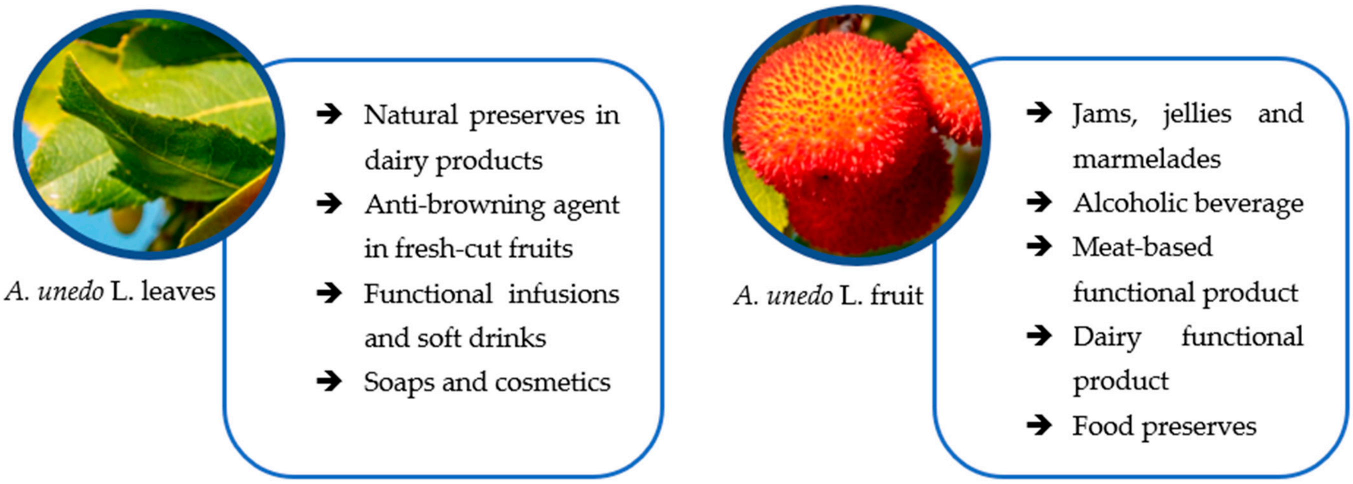

Figure 5. Economic perspective of *A. unedo* L. fruit and leaf utilization [138].

6. Conclusions

With the new trends in the development of functional foods and nutraceuticals, and in line with the emerging global situation influenced by pandemics, ecological problems and energy crises, particular interest of the food (and other) industries for the advanced use of unexploited natural resources is reinforced by the growing of plants. In this context, the strawberry tree (*A. unedo* L.) plant has attracted particular attention and is becoming increasingly appealing to consumers and the industry as a nutrient-rich source of bioactive compounds, with high potential for the production of innovative functional foods and dietary supplements that could greatly contribute to better health. Although both leaves and fruits have significant biological properties, so far, the bioactive compound content and antioxidant activity were significantly higher in the leaves than in fruits.

Although the Mediterranean region is the main growing area for this plant, the strawberry tree has not been sufficiently studied yet. Therefore, future research should focus on fully profiling bioactive constituents and exploring their biological potential in different growing areas to find the species with the greatest potential, and how they can be used in processing. By applying new sustainable manufacturing technologies in the context of Industry 4.0, this plant, whether as fresh or as an extract (both fruits and leaves), could be used in the design of various products. For all of this to be realized in the future, systematic cultivation of this plant would need to be widespread. Therefore, sustainable agronomic practices should be considered to increase cultivation in different geographical regions and to achieve high yields.

Author Contributions: Conceptualization, D.B.K., I.B.K. and B.D.; methodology, A.B.M., K.J., D.L., M.S.B., J.Š.Ž. and P.P.; writing—original draft preparation, A.B.M., I.B.K., M.S.B., B.D., J.Š.Ž. and P.P.; writing—review and editing, A.B.M., I.B.K., K.J., D.L., M.S.B., B.D., J.Š.Ž., P.P. and D.B.K.; visualization, A.B.M. and J.Š.Ž.; supervision, D.B.K.; project administration, D.B.K.; funding acquisition, D.B.K. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Croatian Science Foundation through the funding of the Hurdle Technology and 3D Printing for Sustainable Fruit Juice Processing and Preservation project, IP-2019-04-2105. The work of doctoral student Anica Bebek Markovinović has been fully supported by the "Young researchers' career development project—training of doctoral students" of the Croatian Science Foundation (DOK-2020-01).

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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