

Review

Procyanidins: From Agro-Industrial Waste to Food as Bioactive Molecules

Leidy Johana Valencia-Hernandez ¹, Jorge E. Wong-Paz ², Juan Alberto Ascacio-Valdés ¹,
Mónica L. Chávez-González ¹, Juan Carlos Contreras-Esquivel ¹ and Cristóbal N. Aguilar ^{1,*}

- ¹ Bioprocesses and Bioproducts Research Group, Food Research Department, School of Chemistry, Universidad Autónoma de Coahuila, Unidad Saltillo, Saltillo C.P. 25280, CH, Mexico; johana.valencia@uadec.edu.mx (L.J.V.-H.); alberto_ascaciovaldes@uadec.edu.mx (J.A.A.-V.); monicachavez@uadec.edu.mx (M.L.C.-G.); carlos.contreras@uadec.edu.mx (J.C.C.-E.)
- ² Tecnológico Nacional de México, Instituto Tecnológico de Ciudad Valles, Ciudad Valles C.P. 79010, SL, Mexico; jorge.wong@tecvalles.mx
- * Correspondence: cristobal.aguilar@uadec.edu.mx; Tel.: +52-844-869-0765

Abstract: Procyanidins are an important group of bioactive molecules known for their benefits to human health. These compounds are promising in the treatment of chronic metabolic diseases such as cancer, diabetes, and cardiovascular disease, as they prevent cell damage related to oxidative stress. It is necessary to study effective extraction methods for the recovery of these components. In this review, advances in the recovery of procyanidins from agro-industrial wastes are presented, which are obtained through ultrasound-assisted extraction, microwave-assisted extraction, supercritical fluid extraction, pressurized fluid extraction and subcritical water extraction. Current trends focus on the extraction of procyanidins from seeds, peels, pomaces, leaves and bark in agro-industrial wastes, which are extracted by ultrasound. Some techniques have been coupled with environmentally friendly techniques. There are few studies focused on the extraction and evaluation of biological activities of procyanidins. The identification and quantification of these compounds are the result of the study of the polyphenolic profile of plant sources. Antioxidant, antibiotic, and anti-inflammatory activity are presented as the biological properties of greatest interest. Agro-industrial wastes can be an economical and easily accessible source for the extraction of procyanidins.

Keywords: procyanidins; agro-industrial waste; extraction process; bioactive



Citation: Valencia-Hernandez, L.J.; Wong-Paz, J.E.; Ascacio-Valdés, J.A.; Chávez-González, M.L.; Contreras-Esquivel, J.C.; Aguilar, C.N. Procyanidins: From Agro-industrial Waste to Food as Bioactive Molecules. *Foods* **2021**, *10*, 3152. <https://doi.org/10.3390/foods10123152>

Academic Editors: Frank Dunshea and Hafiz Suleria

Received: 3 September 2021
Accepted: 25 October 2021
Published: 20 December 2021

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Tannins are a class of heterogeneous phytochemicals of high molecular weight (500–3000 Daltons). They represent an important niche market for the food and chemical industry due to their biological potential [1]. Currently, tannins represent an important alternative in the prevention of chronic and degenerative diseases in humans [2,3]. These compounds are produced as a defense strategy of the plant against biotic or abiotic stress factors [1]. In addition, they are associated with growth and development, and reproduction functions in the plant [2,4,5]. Tannins are categorized into two groups: hydrolysable and condensed tannins, according to their chemical structure with respect to the presence of aromatic rings, the number of carbon atoms, and the types of bonds [2–4].

In recent years, condensed tannins, especially procyanidins, have gained importance. These compounds are abundant in nature and are found in vegetables, fruits, legumes, cereals, and seeds of different plant species [6]. In the literature, they are also known as polyphenols with potent biological activities, including anti-carcinogenic, antimicrobial, antiviral, anti-inflammatory, anti-allergic, antimutagenic, and antihyperglycemic effects; they also help to prevent obesity and heart disease problems [7–12].

Agro-industrial wastes are a promising source of procyanidin. Currently, they are discarded at each stage of the food chain. It is estimated that 1.3 billion tons of waste are

discarded, mainly pulp, peel, seed, leaf, stem, bark, and others [13]. Disposal is a significant problem in the industry due to environmental pollution and high costs of handling and transport. To overcome these drawbacks, composting, landfilling, feed, and incineration has been explored [14,15]. However, these wastes have bioactive compounds with potential in pharmaceutical, chemical, and food industries, but sustainable processes at low cost [15] are required for extraction.

Degradative and nondegradative methods have been applied to obtain procyanidins [16]. Procyanidins can be in a soluble or insoluble form, and aqueous solvents can extract the first group. Procyanidins in second group, termed nonextractable, are linked to macromolecules of the cell wall as proteins by glycosidic or ester bonds, for which chemical enzymatic and microbiological methods have been investigated [17,18]. Soluble and low molecular weight procyanidins can be extracted through traditional methods such as maceration, thermal reflux, and organic solvents [19,20]. Disadvantages of these processes include high solvent consumption, highly laborious procedures, long extraction times, and risks to human health [21,22].

Nontraditional extraction methods for nonextractable procyanidins include microwave-assisted extraction, ultrasound-assisted extraction, supercritical fluid extraction, and pressurized liquid extraction, among others. These novel extraction methods are also called green, clean or environmentally friendly methods due to their low solvent consumption and short extraction times, and they also present high compound selectivity and higher compound recovery [22–24].

Procyanidins are considered to be antinutritional compounds of great diversity and structural complexity, which has led to their limited use in the food, agricultural and livestock sectors [25]. For this reason, new recovery processes for obtaining value-added products from natural economic sources have been advanced.

The current survey was performed using academic search systems, including Google Scholar, ScienceDirect, PubMed, Scopus and Web of Science. The search was restricted to only articles in English, where a screening by titles and abstracts was carried out according to the topics of our interest. Inclusion criteria were procyanidins, condensed tannins, agro-industrial wastes, biological activity, and extraction methods. Exclusion criteria were articles on only traditional extraction methods or plant material that is not considered agro-industrial wastes.

In studies published within the years 2009 and 2020, using several keywords including “procyanidins”, “agro-industrial wastes”, “extraction methods”, “bioactive compounds”, “structure” and “biological activity” two central axes were found: procyanidin extraction by extraction type or polyphenolic profile by type of agro-industrial waste and its biological potential. The first axis describes various extraction methods, including solid phase extraction, enzyme-assisted extraction, ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), accelerated solvent extraction (ASE), pressurized liquid extraction (PLE), hot extraction (HE), and heat reflux (HR). The UAE method has been coupled with the enzymatic and percolation method, and the enzymatic method has been carried out with the help of filtration processes. In addition, comparisons are presented between the conventional methods (infusion, maceration, percolation) and the environmentally friendly methods (UAE, MAE, ASE, HE, HR). In this axis three subcategories are presented: effects of extraction variables, optimization of extraction variables and biological activity of these compounds.

The second axis of major interest is the identification, quantification, and analysis of polyphenolic compounds. Several studies mainly used words such as “identification and quantification of polyphenols”, “investigation of the phytochemical composition”, “characterization of the polyphenolic profile” “determination of the chemical composition” “study of the polyphenolic composition” in their proposed objectives. Five subcategories can be detailed in these investigations: biological activity, cytotoxic effects, nutritional composition, method of extraction, industrial or pharmaceutical application. However, there are few documents that have the study of procyanidins as a central objective [26–29].

Other studies present the analysis and extraction of catechin, epicatechin, flavan-3-ols, proanthocyanidins, flavonoids, tannins, and condensed tannins, as part of their central objective [29–32]. From all reviewed papers, only extraction studies of procyanidins and their monomers were included. When the information was poor, studies of condensed tannins were accepted. All the research was on procyanidins or condensed tannins from agro-industrial residues.

Therefore, a review concerning the extraction of procyanidins is required to promote the valorization of agro-industrial wastes. This paper has two main directions. The first is to identify and discuss possible renewable sources of procyanidins and their biological potential. The second is to identify and discuss environmentally friendly extraction strategies for these compounds obtained from agro-industrial wastes. The information found suggests fields for further study and encourages research to continue exploring the discovery of new chemical structures from renewable sources.

2. Polyphenols and Procyanidins: Classification and Chemical Structure

Polyphenols comprise one of the most dominant classes of antioxidant bioactive compounds in nature, also known as phenolic compounds [33]. Usually, the phenolic compounds are distinguished on the base of high molecular weight, presence of hydroxyl groups and aromatic rings, number of carbon atoms, and type of bond [1]. They are classified as flavonoids, phenolic acids, lignans, and stilbenes [34]. Among these, the flavonoids are further divided into six subclasses: flavones, isoflavones, flavanols, flavanones, anthocyanins, and proanthocyanidins [35]. The latter group can also be found in oligomeric or polymeric form, and are soluble or insoluble in water, respectively [36]. The proanthocyanidins consists of structures built by catechin, epicatechin and its gallated forms, which are subdivided into three groups, those consisting of (–)-epiafzelequin are called propelargonidins; and those containing (+)-afzelechin are called prodelfinidins, and procyanidins [3,37]. These categories are proposed according to their degree of oxidation and substitution pattern [38].

Other authors report two main groups of polyphenols: hydrolysable and condensed tannins. Hydrolysable tannins, or polyphenolic nonflavonoids, contain hydroxyl groups that are esterified with gallic or ellagic acid. They have a glucose or polysaccharide molecule in their structure [39]. Condensed tannins, also known as proanthocyanidins, are, after lignin, one of the most abundant groups of phenolic compounds in plants [40,41]. They are characterized by having aromatic rings with hydroxyl groups that allow interactions with proteins and carbohydrates through hydrogen bridges. These interactions dependent of bond types (interflavonics), molar mass, galloyl groups and modification of the phenyl hydroxyl groups [40,42]. Because of this, different conformations can be formed in the procyanidin structure, resulting in highly complex molecules with different functional characteristics [3,4,43].

Procyanidins are derived from the group of proanthocyanidins, being the most prominent of this group in plants [44]. They are considered heterogenous compounds due to their diverse chemical structure [45]. These molecules contain flavan-3-ol monomers as basic units in their structure, which are composed exclusively of (+) catechin and (–) epicatechin. (Epi)catechin monomers may be biosynthetic precursors of procyanidins [46–49]. The type of monomer formed depends on the type of residue present in the structure, such as resorcinol and phloroglucinol, and are present in ring A, with catechol or pyrogallol in-ring B [5]. These compounds can be classified according to chemical structure, hydroxylation pattern and stereochemistry, into oligomers and polymers that can be grouped in three groups by their degree of polymerization (DP), i.e., monomers with DP equal to 1, oligomers with DPs between 2 and 10 and the polymers with DPs higher than 10 [50]. Thus, according to the DP there are monomers, dimers, trimers, and tetramers of procyanidins, corresponding to 1, 2, 3 and 4 base units, respectively [3,42,44]. Among the dimeric and trimeric procyanidins, A1, B1, B2, B3, B4, B8, C1 and T2 have been identified, the last two belonging to the group of trimeric procyanidins [40].

Procyanidins possess interflavan bonds in the asymmetric carbons C2 and C3, C4-C8 and C4-C6 [49]. According to the nature of the bond, they can be further classified into type A and B procyanidins. A-type procyanidins contain a double interflavanoid linkage C-C (C4-C8/C6) and an additional ether bond (C2-O-C7 or C2-O-C5); these procyanidins may result from additional oxidation reactions of B-type procyanidin dimers [36,43,51,52]. B-type procyanidins contain interflavanic bonds that are covalently linked in carbon C-4-C-8 or C-4-C-6, where the latter are more prevalent than A-type procyanidins. Figures 1 and 2 shows examples of dimeric procyanidins of type A and B, respectively.

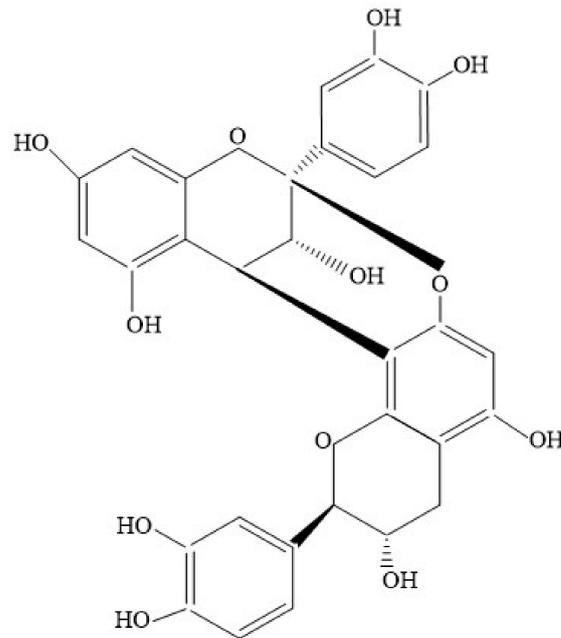


Figure 1. Structure of A1-type dimer procyanidins linked with double C4 → C8 and C2-O-C7 linkage.

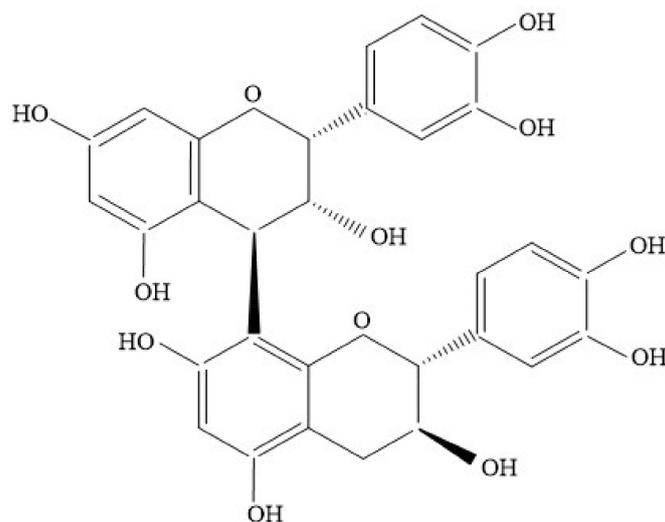


Figure 2. Structure of B1-type dimer procyanidin linked with a single C4 → C8.

3. Agro-Industrial Wastes and Procyanidins

3.1. Generation of Agro-Industrial Wastes

The idea of zero-waste has been proposed in production chains, and various investigations have indicated the conversion of these wastes to value-added by-products such as antioxidants, prebiotic ingredients, antimicrobial agents, enzymes, proteins, colorants, bioplastics, and biofuels [45]. The food and nonfood processing industry generates many

agro-industrial wastes, including agricultural vegetal and forestry wood, estimated at 55 million tons in 2016 for the European Union [53]. In developed countries, waste is calculated at approximately 0.5 million tons of fruits and vegetables generated in the food industry and establishments serving and distributing. Moreover, fruit and vegetable waste represents 60% of the waste generated annually worldwide [54]. These residues have a wide range of polyphenolic compounds with biological activities [55]. Knowledge of the availability and quantity of these vegetal materials is indispensable for the development and research of reuse strategies. However, accurate data on all waste generated worldwide in each production process remains to be explored [56].

Several studies have been conducted to extract and recover bioactive compounds from agro-industrial wastes which can generate value-added products in different production chains while preserving environmental balance. The agro-industrial wastes commonly indicated in the literature correspond to the production chains of coffee, cocoa, wood, processed foods, and fruit (grapes, apples, limes, cranberries, lychee, avocado, noni, pineapple) [57,58]. This last category covers considerable amounts of residues due to the wide range of food products demanded by the market through the processing of fruit crops. It is estimated that more than 50% of the mass of the fruit is used in obtaining beverages, juices, concentrates, jams, sauces, and minimally processed products, with the remaining percentage corresponds to agro-industrial waste [59]. One of the most important crops is grapes, with an annual production of 74.3 million metric tons, where it is estimated that between 15% and 20% is generated as waste. In the case of blueberries, it has been considered that 96% of mass is used for manufacturing in the industry, in sour cherry about 85% used for the production of juices jams, fruit juices and frozen fruit [59]. From these processes peels and seeds are discarded as the main by-products, which are not edible but are rich sources of bioactive molecules [60].

Other types of waste are from fermentation processes in the production of cocoa and coffee. In 2017, the international cocoa organization reported the production of 600 tons of cocoa shell [59]. The wastes generated during forestry activities, such as skins, shells, husks, leaves, flowers and stems, contain bioactive compounds [45]. Commonly they have been used in organic fertilization, composting, energy generation, incineration, animal feed and landfilling [14]. The latest studies on obtaining bioactive compounds have been directed to the compositional and nutritional analysis of new sources of isolation from *Receptaculum nelumbinis*, *Acer truncatum* (leaves, stems and bark), *Euterpe oleracea* (seeds), *Zanthoxylum bungeanum* (pericarps), *Hawthorn crataegus* (Flowers, leaves), *Coniza banariensis* (leaves), *Vulgaris monocarpa* (leaves and roots), *Rhodiola rosea* (rhizome), *Prunus spinosa* (flowers), *Elsholtzia ciliata*, *Fagopyrum tataricum* (flowers leaves, stalk and roots), among others.

The search for natural sources of antioxidants and other biological properties for the benefit of human health has been a priority. One of the most important benefits reported in the literature is antiproliferative activity against cancer cells and the ability to scavenge free radicals [61–63]. However, in the literature, information on procyanidins from agro-industrial wastes, their distribution, yields in extraction, and biological activity need to be summarized and specified.

3.2. Occurrence of Procyanidins in Agro-Industrial Wastes and their Biological Potential

Procyanidins and their monomers have been identified in several agro-industrial wastes from the food processing industries such as cocoa, berries, grapes, apples, litchi, blueberries, plums, avocado, nuts, tea leaves, coffee, cinnamon, peanut, leguminous plants, and several other wastes, as illustrated in Table 1 [38,44,64–70]. Among the main parts of the plant that are considered agro-industrial wastes and do not conflict with human food include leaves, flowers, stems, roots, bark, skin, pomace, pulp, and seed. These compounds have been found in a high percentage in seeds and berry skins. In Saskatoon berry peel, 53% of the total polyphenols are polymeric procyanidins. Moreover, the highest antioxidant activity was found in the peel, which was 16 and 5 times higher

than in seeds and pulp, respectively [71]. Studies have focused on the characterization and quantification of bioactive components in baobab, a tree of African origin, concerning obtaining procyanidins; yields corresponding to 100.1 mg/100 g were reported [72]. Similar studies were carried out by Tembo et al. [73], who demonstrated that the antioxidant activity was correlated with the total phenolic content, procyanidin B2, and vitamin C.

Research indicated the presence of procyanidins in the pericarp of lychee, a residue that represents 15% of total fresh fruit weight. Miranda-Hernández et al. [74] reported percentages between 65–70% using methanol and acetone (70% v/v) as the solvent for extraction. Wong-Paz et al. [75] extracted procyanidins from coffee pulp with a concentration of 98.6% in extractions with acetone (70% v/v). Luo et al. [76] developed a method for obtaining high purity procyanidins (90%) in grape skins and seeds, achieving maximum yields of 4.1 and 13.6 mg, respectively. Other authors reported a yield of 3.94 mg of procyanidin (catechin equivalents)/gram of dried sea buckthorn seed [77]. The procyanidin content may vary according to the origin and variety of the plant material. For example, in coffee hulls, the highest procyanidin content was found in samples of the Robusta variety from India and Arabica from Mexico with 534 and 260 µg/g, respectively [78]. Authors suggest that the differences found may be due to factors such as geographic location, average temperature and irradiation level [79].

On the other hand, another topic of interest is the correlation of biological activity with the structural and chemical characteristics of procyanidins. In previous studies, the correlation of molecular weight and antioxidant activity of phenolic compounds from *Choerospondias axillaris* peel residues was determined by cellular and chemical tests, with a decrease in this biological activity occurring with an increase of molecular weight in cell assays with proanthocyanidins, while for spectrophotometric chemical assays, an increase in this variable was observed [80]. Other works report different biological activities of extracts from *Tectaria coadunata* rhizomes obtained with methanol and ethyl acetate, finding inhibitory enzyme activity (amylase and tyrosinase) associated with degenerative diseases and anticancer activity in ethyl acetate fractions. Anti-invasive and anti-proliferative activity in pancreatic cancer cell lines was also found. The highest procyanidin yields were found in the polymeric (85.46 mg/g) and trimeric (57.79 mg/g) fractions corresponding to the extractions performed with methanol and ethyl acetate, respectively [81]. A recent finding in laurel wood extracts demonstrated that B-type dimer and A type trimer procyanidins exhibited antimicrobial and antibiofilm activity [82]. Procyanidin of *Annona crassiflora* fruit peel show antiglycation capacities [83]. From *Vaccinium meridionale* Swartz pomace was obtained A-type procyanidin, demonstrating its effectiveness in the control of pathogenic bacteria [84].

Table 1. Sources of procyanidins from agro-industrial wastes.

Plant	Waste Type	Compound Type	Concentration	Reference
<i>Artocarpus heterophyllus</i> Lam		PCB	-	[85]
<i>Choerospondias axillaris</i>		PCB2	390 mg/g extract	[86]
<i>Musa</i> AAA	Peel	C, EC, PCs: B1, B2 and B4	-	[87]
<i>Passiflora ligularis</i> and <i>P. edulis</i> , <i>P. mollissima</i>		PCs: dimers and trimers	-	[88]
<i>Litchi chinensis</i>	Pericarp	PCs: A and B	-	[74]
<i>Litchi chinensis</i> Sonn		PCO	-	[76]
<i>Vitis vinifera</i> L.	Pomace	PCs: B1, B2	4.8–4.3 µg/kg extract	[89]

Table 1. Cont.

Plant.	Waste Type	Compound Type	Concentration	Reference
<i>Apocynum venetum</i>		PCB2	13.4 ug/mL	[90]
<i>Persea americana</i>		PCB	-	[91]
<i>Combretum mucronatum</i>		EC, PCs: B2, B5, C1, D1	-	[92]
<i>Moringa oleifera</i>	Leaf	PCB7 (dimer)	-	[93]
<i>Litchi chinensis</i>		EC, PCA2	14.8–44.5 and 44.8–69.6 mg/g extract	[94]
<i>Psidium guajava</i> L.		PCs	-	[95]
<i>Psidium guajava</i> L.		PCs	-	[95]
<i>Vaccinium myrtillus</i> L.	Leaf and stem	EC and PCB2, respectively	-	[96]
<i>Vaccinium vitis-idaea</i> L.		C, PCs: A, B, dimers, trimers	-	[85]
<i>Crataegus</i> spp	Leaf and flower	PCO	-	[97]
<i>Juglans regia</i>		PCA		[98]
<i>Crataegus monogyna</i>	Flower	PCO	-	[97]
<i>Tilia</i> sp		PCs	-	[99]
<i>Trifolium pratense</i>		PCs	-	[99]
<i>Vitis vinifera</i> L.		PCB2	0.41–1.6 mg/g extract	[100]
<i>Vitis vinifera</i> L.	Seed	PCs: B1, B3, B6, B4, B2, B7, B5	-	[101]
<i>Vitis vinifera</i> L.		PCs	-	[99]
<i>Euterpe oleracea</i>		C, EC, PCB1	-	[95]
<i>Amelanchier alnifolia</i> Nutt	Seed and peel	PCP	1189.76–2631.73 mg/100 g extract	[71]
<i>Cinnamomum cassia</i>		PCs: A, B	-	[18]
<i>Aronia melanocarpa</i>	Bark	PCs: B2, B5, C1	-	[102]
<i>Fagus sylvatica</i> L.		C, EC, PCs: B, C.	-	[103]
<i>Calliandra haematocephala</i>		CT	841 mg/g extract	[104]
<i>Laurus nobilis</i> L.	Wood	PCB2	-	[82]
<i>Saraca asoca</i>	Stem and root	PCB2	-	[105]
<i>Coffea Arabica</i>	Pulp	PCs: B2, A (trimer), C1, tetramer, pentamer,	-	[75]
<i>Theobroma cacao</i> L.	Hulls	PCs: B1, B2	0.55–0.83 and 0.23–0.9 mg/g extract	[106]
<i>Elsholtzia ciliata</i>	Aerial parts	PCB	-	[107]
<i>Pyrus communis</i>	Ripe and over-ripe pears	PCs (low DP)	-	[108]

Other studies suggest that the biological activities of these compounds depend on their structure, degree of polymerization, and their degree of galloylation [109]. The degree of polymerization determines their bioavailability and their ability to be adsorbed into the blood. Some studies indicate that oligomeric procyanidins are more absorbable than polymeric procyanidins [110–112]. Antioxidant activity has been reported to depend on the presence of the catechol group of some procyanidins, which acts as a donor of hydrogen atoms to free radicals. Other authors indicate that such activity depends directly on the number of hydroxyl groups present in the structure, which increases with the

polymerization of the molecule [113,114]. In a previous study, the antidiabetic activity of oligomeric procyanidins types A and B from litchi pericarp was evaluated in tests with mice, finding the best results in type A procyanidin [115]. Oligomeric procyanidins are more effective in capturing free radicals and superoxide anions, as well as in weight control and blood glucose regulation in tests with mice [12,116]. In polymeric procyanidins, it has been verified that a protective effect against oxidative damage in hepatic cells occurred, as well as a reduction of cholesterol and fatty acid in diabetic mice [117,118]. Other studies indicated that procyanidin C1 from grape seed could prevent neurodegenerative diseases, and its antioxidant activity was verified [119].

Procyanidins are of economic interest due to their antioxidant [120], anti-inflammatory [121], antidiabetic [122], anti-aging, neuroprotective, cardioprotective [123], antiviral, and antimicrobial effects [124,125]. These biological properties allow the generation of value-added products for the pharmaceutical, food and cosmetic industries [109]. Table 2 summarizes some relevant advances in the biological activity of procyanidins from different types of agro-industrial wastes. Early studies demonstrated that grape seeds, which are source of C1-type procyanidins, showed a neuroprotective effect [119]. Forestry waste such as leaves, roots, and bark from *Annona muricata* [126], *Paullinia pinnata* [127] and *Albizia odoratissima* [128] have an inhibitory effect in lipid peroxidation, pathogen growth of plants and cancer cell proliferation, respectively. Other biological activities such as anti-VIH, anti-inflammatory, antiwrinkle effects are reported for *Cinnamomum zylanicum* [129], coffee pulp [130], and cocoa pods [46], respectively. Commercial sources obtained from grape seed have the potential for treatment of cardiovascular diseases and obesity control [131].

Table 2. Biological activity of procyanidins obtained from agro-industrial wastes, and possible applications.

Agro-Industrial Waste	Procyanidin Type	Application Potential/Attributes	Assay Type	Biological Activity	Reference
<i>Alectryon oleifolius</i>	PCA2	Control programs of <i>Cyathostomin</i>	In Vitro	Anthelmintic activity in larval	[132]
<i>Cinnamomum zeylanicum</i> bark	PCA (commercial compound of Indus Biotech Private Limited, Pune, India)	-	In Vivo (animals)	Anti-allergic	[133]
<i>Rhododendron formosanum</i> leaves	PCC4 and cinnamtannin D1	Development of pharmaceutical products	In Vitro	Antibacterial, and pleiotropic effects	[134]
<i>Theobroma cacao</i> L. pods	PCs: dimer B1 and trimer C2	Functional cosmetic	In Vitro	Antioxidant and anti-wrinkles	[135]
<i>Punica granatum</i> L. peel	C, EC, dimer A, dimer B1, dimer B2, dimer B3, trimer A	-	In Vitro	Antioxidant, inhibition of α -glucosidase activity, lipase activity, LDL-cholesterol oxidation	[46]
<i>Cinamomum Zylanicum</i> bark	PC A (trimers and pentamers)	-	In Vitro	Anti-VIH-1	[8]
<i>Vitis vinifera</i> seed	PCB1	Cancer chemoprevention, antineoplastic agent, cardiovascular benefit	In Vitro/In Vivo (animals)	Inhibition of cyclooxygenase-2 and enhance prostacyclin	[9]
<i>Potentilla erecta</i> L. rhizome	PCB	-	In Vivo (animals)	Antithrombotic	[115]
<i>Garcinia mangostana</i> pericarp	Monomers, dimers, and PCO	-Ingredient in chocolate processing -Nutritional and sensory quality	In Vitro	-	[136]
<i>Paullinia pinnata</i> L. Roots	C, EC, and PCs: trimeric A, tetrameric A, and PCP.	-	In Vitro	Anthelmintic	[127]

Table 2. Cont.

Agro-Industrial Waste	Procyanidin Type	Application Potential/Attributes	Assay Type	Biological Activity	Reference
<i>Theobroma cacao</i> L. powder	C, and PCB2	Treatment against cancer	In Vitro	Cytotoxic effect in ovarian cancer cell, impact the regular cell cycle progression of cancer and overcoming drug resistance	[135]
<i>Litchi chinensis</i> pericarp	PCO: A-type	-	In Vitro	Hypoglycemic	[137]
<i>Acacia mearnsii</i> leaves	PC: dimer B	-	In Vitro	Anti-inflammatory and antioxidant	[138]
<i>Larix decidua</i> bark	C, EC, and PCs: B2, trimer B, and tetramer B	-	In Vitro	Antioxidant	[139]
<i>Clausena lansium</i> pericarp	C, EC PC with DP up to the 20-mers.	Chelating ability	In Vitro	Inhibition on the melanogenic activity in B16 anti-tyrosinase	[140]
<i>Litchi chinensis</i> pericarp	PCA2	Therapy of liver damage	In Vitro/In Vivo (animals)	Antioxidant	[141]
<i>Annona crassiflora</i> peel	C, EC and PC B2	Treatment of diabetes	In Vitro	Antioxidant, hepatoprotective effect, influence glutathione reductase activity and glutathione level.	[142]
<i>Vitis vinifera</i> seed	C, EC, and PCs: dimer B1, dimer B2, dimer B5, dimer B2 gallate, trimer C1, trimer T2, tetramer A2, unknown dimers, pentamers, and hexamers	-	In Vitro	Antimicrobial	[143]
<i>Triplaris gardneriana</i> seeds	C, PCs: dimer B, digalloylated PC PCB, monogalloylated procyanidin dimer B	Rapid biotransformation	In Vitro	Antioxidant	[144]
<i>Schinus terebinthifolia</i> Stems	PCB	Treatment of Herpes simplex virus type infections	In Vitro/In Vivo (animals)	Antiviral	[145]
<i>Larix gmelini</i> bark	PCs	Healthcare, and cosmetic products	In Vitro	Antimicrobial, affects membrane protein synthesis of <i>Staphylococcus aureus</i>	[146]
<i>Paullinia cupana</i>	PCs	Prevention and control of <i>Helicobacter pylori</i>	In Vitro	Antioxidant and gastroprotective activity	[144]
<i>Tamarindus indica</i> seed coat	Mixture of procyanidins	Treatment therapeutics	In Vitro	Antioxidant	[145]
<i>Vitis vinifera</i> pomace	PCs: dimer, trimer C1 and trimer (possible C2)	-	In Vitro/In Vivo (animals)	Antioxidant, enhancement of catalase and glutathione peroxidase activity in colon. Enhancement of superoxide dismutase activity in duodenum	[147]
Juice from Unripe <i>Vitis vinifera</i>	C, EC and PCs: B1 and B2.	-	In Vitro	Antioxidant and Anti-browning	[148]

Table 2. Cont.

Agro-Industrial Waste	Procyanidin Type	Application Potential/Attributes	Assay Type	Biological Activity	Reference
<i>Annona muricata</i> leaves	EC, and PCs: B2 and C1	Treatments in diabetes mellitus	In Vitro	Antioxidant, inhibitory activities against advanced glycation end-product formation, pancreatic lipase, α -amylase, α -glucosidase, and lipid peroxidation	[129]
<i>Vitis vinifera</i> seed	PCB2 3,3"-di-O-gallate	Control malignant cells in prostate	In Vitro	Inhibition MAP kinase phosphatase	[149]
Commercial (<i>Vitis vinifera</i> seed)	PCs dimers	Potential in cardiovascular and obesity treatment	In Vivo (animals)	Reduces adiposity and oxidative stress in the heart	[150]
<i>Coffea arabica</i> L. pulp	PCs: dimers and trimers		In Vitro	Anti-inflammatory and inhibition interleukin-8 release in human gastric epithelial cells	[151]
<i>Trichilia catigua</i> bark	PCB2–8-C-rhamnoside, PCB2 (epi)-catechin—(epi)-catechin	Potential as antifatigue drug	In Vivo (animals)	Antioxidant, anticholinesterase,	[149]
<i>Calluna vulgaris</i> L. flowers	Proanthocyanidins	Food ingredient	In Vitro	Antioxidant and antimicrobial	[152]
<i>Persea americana</i> peel and seed	C, EC, and PCs: B1 and B2,	-	In Vitro	Antioxidant and anti-inflammatory	[153]
<i>Persimmon</i> vinegar pulp	PCA2	-	In Vitro	Hepato-protective effects	[154]
Stem bark of <i>Detarium microcarpum</i> , <i>Cassia siamea</i> , and <i>Guiera senegalensis</i>	PCB3	Anti-breast cancer agents	In Vitro	Antioxidant, and antiproliferative effects on cancer cells	[155]
Leaves and stem bark of <i>Ficus curtipes</i>	C, EC and PCs: B2 and C	-	In Vitro	Anti-inflammatory and modulation of nitric oxide synthase enzyme expression	[156]
<i>Fraxinus angustifolia</i>	C and PCB1	Regulation of signaling pathways homeostasis	In Vitro	Antioxidant and anti-inflammatory	[157]
<i>Nelumbo nucifera</i> seed epicarp	PC with of epicatechin units linked by B-type interflavan bonds	-	In Vitro	Antioxidant and anti- α -amylase	[158]
Commercial standard of Sigma-Aldrich, Merck KGaA	PCB2	-		Inhibition of angiogenesis, fibrogenesis processes, Inhibition of proliferation and induction apoptosis of human hepatic stellate cell	[156]
<i>Vitis vinifera</i> marc	C, EC, and PC trimer	Thermal stability	In Vitro	Antioxidant	[159]
Commercial of Extrasynthese (Genay, France)	PC s: A2 and B2, and cinnamtannin B-1	Prevention of urinary tract infections	In Vitro	Antiadhesive of uropathogens	[160]
<i>Vitis vinifera</i> seed and pine bark	C, EC, PCs: dimers 1, 2, B1, B2, and B5, trimers 1, 2, 3 and C1, tetramer 1, pentamer 1 and 2, hexamer 1 and 2, heptamer 1 and 2, octamer, decamer, dimer gallate and dimer B2 gallate	-	In Vivo (animals)	Enhances cytokine production	[161]

Table 2. Cont.

Agro-Industrial Waste	Procyanidin Type	Application Potential/Attributes	Assay Type	Biological Activity	Reference
<i>Melastoma malabathricum</i> leaves	PCA	-	In Vivo (animals)	Cytotoxic effect against colon cancer cells	[162]
<i>Albezia odoratissima</i> bark	PCC1	-	In Vitro	Anticancer in breast	[131]
<i>Feijoa sellowiana</i> leaves	C, PCs: dimer B1, B2 and B3, galloyled procyanidin dimer, digalloyled PC dimer	-	In Vitro	Inhibition of acetylcholinesterase and antilipase activity	[163]
Residual cake of <i>Pistacia vera</i> L.	C, EC, and PCs: B1, B2, and galloylated dimer	-	In Vitro	Antioxidant	[128]
<i>Vitis vinifera</i> seed	PCC1	Application for neurological disorders	In Vitro	Antioxidant, neuroprotective	[164]
Skin, seed, skin, and bunch stem of <i>Vitis vinifera</i>	PC tetramer (crown PC), PCO, PCP	-	In Vitro	Inhibition of amyloid- β peptide	[162]

4. Extraction of Procyanidins from Agro-Industrial Wastes

Extraction methods have been used to recover bioactive phytochemicals from natural sources, which are of interest in human health. These methods were previously required to separate, purify and analyze bioactive compounds of plants [163] and are referred to in the literature as conventional or traditional or classical methods, among them being maceration (M), percolation (P) and successive solvent extraction (SSE). These methods have been widely used in the extraction of procyanidins. Some authors report procyanidin extraction from different food production chains, for example, raw cacao and blueberry [164,165]. However, researchers have proposed alternative methods that allow higher compound yields, process efficiency, and lower solvent use. Efficiency is an important factor in choosing the extraction method, being related to the recovery of compounds and biological stability of compounds, time, and energy-saving during the extraction process. Efficiency depends on the conditions of extraction, which could affect the structure of compounds as location and distribution of hydroxyl groups, terminal and extension units, interflavanic bonds, and interactions with other compounds [166,167]. This review focuses on eco-friendly recovery methods of proanthocyanidins, procyanidins, and monomeric and polymeric forms through UAE, MAE, supercritical fluid extraction (SFE), PLE and subcritical water extraction (SWE) (Table 3).

Table 3. Research on extraction of procyanidins from agro-industrial wastes, and future applications.

Plant/Waste	Technique	Conditions *	Type de Procyanidin or Yield	Type of Application	Reference
<i>Vitis vinifera</i> /skin	SSE and UAE	5 g/100 mL Methanol 60% Solution acidified water pH 1.5	-	Conservation of food	[168]
<i>Vaccinium macrocarpon</i> /pomace	SSE	-Hexane 40 mL, centrifugation 10 min at 10,864× g. -Ethyl acetate (40 mL), and centrifugation for 10 min at 10,864× g. -Neutralization and mixing with 20 mL of acetone/water/acetic acid, (70:29.5:0.5 v/v/v), homogenization for 1 min. -All treatments at 25, 40 and 60 °C.	519.3 mg of PC/100 g DM at 60 °C.	Nutraceutical, estimation method of PC	[111]
<i>Malus domestica</i> /pomace	Enzymatic maceration	Pectinex (20 mL/100 kg sample), stirring 1 h at 20 °C.	-PCs: B1 (18.7 mg/mL), B2 (80.2 mg/mL), and C1 (18.7%). -PCP: 57 and 24% corresponding to total polyphenols in pomace and fresh juices, respectively.	Production of beverages and drinks	[169]
<i>Betula pendula</i> /bark	SSE	Methanol (8%)-Water.	PC (dimer)	Isolated procyanidin glycosides (rarely found in nature)	[170]
<i>Vitis vinifera</i> (Wine waste)/seed, skin, pomace	SSE	Acetone (50%)-water, ethanol (50%)-water, Methanol (50%)-water.	PCs: A and B	Antioxidant activity	[171]

Table 3. Cont.

Plant/Waste	Technique	Conditions *	Type de Procyanidin or Yield	Type of Application	Reference
<i>Pinus pinaster</i> /bark	High pressure solvent (HPE)	-CO ₂ , CO ₂ -ethanol (90:10), 3 times, 323 and 303 °C, 20.3 and 25.1 MPa, 370 and 360 min; 7.6, 13.2, and 19.1 kg/s × 10 ⁵ , solvent-to-solid mass ratio 28:1, 2:1, 20:1. -CO ₂ -ethanol (90:10) 3 times, 303 °C, 25.1 MPa, 360 min; 7.6, 13.2, and 19.1 kg/s × 10 ⁵ , solvent-to-solid mass ratio 28:1, 2:1, 20:1. -CO ₂ -ethanol (70:30), CO ₂ -ethanol (50:50), CO ₂ -ethanol (30:70) and CO ₂ -ethanol (10:90); 303 °C, 25.1 MPa, 210 min; 7.6 kg/s × 10 ⁵ , solvent-to-solid mass ratio 28:1, 2:1, 20:1.	19.8 % (mg CME **/mg extract × 100 dried base). The best result was achieved with CO ₂ -ethanol (70:30) with Flow rate of 7.6 kg/s treatments.	Improved extraction methodologies	[172]
<i>Malus domestica</i> /pomace	* 1. M, 2. PLE, 3. UAE, 4. MAE	1. Solid-solvent ratio (ethanol) 1 g/1 mL, stirred 1 h, room temperature. 2. Ethanol, 3 min 40 °C, 100 bar, 3 cycles. 3. Relation solute—solvent (ethanol) 3 g/60 mL, 30 min, room temperature. 4. Solid-solvent ratio (ethanol ethyl acetate or water/methanol) 1 g/20 mL, 3 s, 3 cycles, 1000 W.	PC (dimer), best results: MAE (ethanol or ethyl acetate).	Antioxidant activity	[173]
<i>Larix gmelinii</i> /bark, xilem	UAE	Bath power 250 W, Solute-solvent ratio 5 g/100 mL ethanol (50%), 0.5 h.	601.94 mg PC/g bark (North orientation)	Use of wood in industrial process.	[151]
<i>Coffea arabica</i> L./pulp	* 1. UAE, 2. M	1. Ethanol-water (70:30), water-ethanol (30:70), 100% milliQwarer, Power 100 W, 30 min, room temperature in the dark. 2. Ethanol-water (70:30), water-ethanol (30:70), 100% milliQwarer, 16 h, room temperature in the dark.	PC A (dimers and trimers) obtained with UAE.	Food supplements	[174]

Table 3. Cont.

Plant/Waste	Technique	Conditions *	Type de Procyanidin or Yield	Type of Application	Reference
<i>Theobroma cacao</i> /bean shell	PLE	Solvent-to-solid ratio 1:3, 60, 70 and 90 °C, 5–50 min, 10.35 Mpa.	Yield: 0.73 mg PC B2/g dried cocoa Shell (60 °C, 50 min)	Antioxidant activity	[73]
<i>Acer truncatum</i> /seed coat	SSE	Solution with 20 g of sample, water, ethanol (100%), aqueous acetone (70%), acetone (100%), aqueous ethanol (70%), and aqueous ethanol (40%), 30 min, centrifugation 6000 rpm by 10 min.	PC (dimer, trimer, tetramer, pentamer)	New phytochemical	[75]
<i>Vitis vinifera</i> (Wine waste)/seed, stem skin, pomace	MAE	Power 98 W, 24 °C, Ethanol (10 mL), extraction time 5–15 min, vegetal sample 1–2 g.	PC (trimer)	Formulations of food, chemical, pharmaceutical products	[157,175]
<i>Theobroma cacao</i> /bean shell	* 1. UAE, 2. Hydrodynamic cavitation (HC)	1. -Hexane, 40 °C, 15 min -Solvent-to-solid ratio 70:30 (ethanol/Water). -Solvent-to-solid ratio 30:49:21 (Hexane/ethanol/water). 2. Ethanol/Water 3000 rpm, 11 min, cycles 47.1, cycle times 5 s, residence time 5 s, adsorbed energy 6.82 KW.	PC for HC	Process design	[175]
<i>Malus domestica</i> /parenquima, skim	SSE	Hexane, methanol/acetic acid (99:1 v/v), Acetone/water/acetic acid (60:39:1 v/v/v).	PC with a DP 9	Formulations of juices	[176]
<i>Vitis vinifera</i> /seed	SSE	Ethanol/water (1:1, v/v), stirring 30 min in the dark.	PCB (dimer and tetramer)	Nutraceutical products	[27]
<i>Theobroma cacao</i> L./bean shell	* 1. MAE, 2. SSE	1. Power 500 W, heating rate 20 °C/min, 400 rpm, initial solid-solvent ratio 6 g/250 mL water, solid/liquid ratio 0.030, 0.045, 0.060 g/mL, extraction time 5, 15, 25 min and at 70, 85, 100 °C. 2. Solid/liquid ratio 0.045 g/mL, 100 °C, 90 min, centrifugation 5300 rpm, 25 min.	Polyphenols 35.9 mg GAE/g.	Food additives, food packaging	[177]

Table 3. Cont.

Plant/Waste	Technique	Conditions *	Type de Procyanidin or Yield	Type of Application	Reference
<i>Malus domestica</i> /pomace	SSE	-Diethyl ether/ethyl acetate (DE/AE) (1:1, v/v), Acid hydrolysis (pH 2). -DE/AE (1:1, v/v), base hydrolysis (pH 2). -Methanol (80%)-Water, 1% acid formic, exposition 2 times.	PC B2	Functional products	[178]
<i>Vaccinium</i> /pomace	* 1. PLE—Ethanol 2. PLE—Water	1. 83 °C, 15 min, °C, 3 cycles. 2. 130 °C, 10 min, °C, 3 cycles.	198.5 and 532.2 mg of proanthocyanidins/g. Recovery of dimer PCB2 (578.5 Daltons)	Processing residue at industrial level.	[176]

* The numbers correspond to the conditions in each type of extraction described in the table. ** CME: (+)-catechin monohydrated equivalents.

4.1. Ultrasound-Assisted Extraction

Ultrasound-assisted extraction (UAE) is a simple method with short duration and has little effect on the environment. It is considered an emerging technology and better than classical methods due to rapid mass production [177]. This type of extraction has several applications in various industries (agro-industrial wastes) to obtain polyphenols such as procyanidins [107]. For the extraction of procyanidins from by-products of wine processing, UAE has been used to study its effect on the compounds' structure and biological activity.

Extraction obtaining bioactive compounds by the ultrasound method from agro-industrial residues has been widely reported [164,179]. However, few reports of procyanidin extraction have been reported in the last five years, and most studies have focused on the evaluation of different extraction conditions on the yields of bioactive compounds [164,180–186]. The mechanism of extraction occurs by mechanical vibration through waves that penetrate a liquid system and form gas bubbles [187]. These bubbles are affected by the acoustic cavitation phenomenon, which leads to their collapse. Thus, there is an increase in pressure and temperature in the medium that creates an ultrasound micro-jet in the solution [188].

Grape seeds are rich sources of oligomeric procyanidins, rather than polymeric procyanidins, which represents an advantage for different industries. The ultrasound technique was used to study the depolymerization of procyanidins, finding considerable increases in the content of polymeric procyanidins, oligomeric and catechin monomers, corresponding to 41%, 35% and 49%, respectively [189].

Researchers also used this technique by varying the frequency of the test (45 and 20 kHz), obtaining higher polymeric procyanidin concentrations at 20 kHz. The breakdown of procyanidins was expected in tests with the frequency change. However, at 45 kHz the concentration of procyanidins decreased, due to obstructions in the mass transfer that occurred during the bubble formation. The improved antioxidant activity in treatments with ultrasound was associated with the hydroxyl groups, which were identified by Fourier transform infrared spectroscopy (FTIR) analysis, and could be generated by the rupture of links between procyanidins with polysaccharides or proteins [189].

A modification to the UAE is called the high-intensity ultrasound (HIUS) technique that is characterized by working at high intensity and low-frequency conditions. HIUS is attractive because of production costs, simplicity, reduced extraction times and small environment effect. Applying ultrasound of high intensity on *Araticum* peel extracts increased antioxidant activity of procyanidins A and B. These the results were achieved with short extraction times (0.5–5.0 min) [190].

Recently, combination with cavitation methods using negative pressure has been proposed to increase the yields of procyanidins, by increasing ultrasonic power between 0.2–0.35 W/cm². A combination of nitrogen pressure on cavitation, collision of bubbles, cell disruption, and transfer of compounds in the extracting medium during extraction improved the yields of compounds, [164,191]. Other process conditions could affect the biological activity of procyanidins, such as vegetal material concentration, type of solvent, temperature, stirring speed, and time stirring [192,193]. Improvement of the bioavailability of procyanidins for pharmaceutical purposes has led to the development of methods for controlling the particle size of the compounds. To this goal, ultrasonic methods have been combined with the precipitation of antisolvents, with successful results under the optimal parameters of power, stirring speed, stirring of 620 W, 760 r/min, 14 min and 0.3 mg/mL, respectively, which allowed increase antioxidant activity. This may be due to the phenomenon of collision of particles by cavitation and a decrease in the agglomeration of crystals [192].

Recent advances in UAE have been explored using a macroporous resin to improve the purification and recovery of bioactive compounds, including procyanidins. The combination of these methods helps to increase extraction yield and reduce process times. The main factors that influence the quantification of the extraction process are the structure, polarity, and size of a bioactive molecule, type of resin, solution concentration, interac-

tion resin-molecule, and ultrasound power [194]. A previous study confirmed that the employed resins (HPD-500) in ultrasonic treatments, when applied at 270–540 W for 15 and 5 min, respectively, increased adsorption capacity and mass transfer of procyanidins from baobab fruit pulp, as compared to treatments without use of ultrasound. In this study, procyanidins B2 and C1 were identified and quantified in samples treated at high power sonication (540 W) and short exposure time (5 min), with concentrations corresponding to 751.34 ± 32.76 mg/100 g dry matter (DM) and 566.38 ± 10.78 mg/100 g DM, respectively [193]. Limwachiranon et al. [180] reported procyanidin concentrations of 20 mg in lotus seed extracts using mixed solvents (acetic acid, acetone, and water).

Another type of combination with the ultrasound technique is the use of enzymes. Research has been carried out to obtain more available bioactive compounds using enzymes in ultrasound extractions using methanol as a solvent. Martins et al. [149] studied the biotransformation of condensed tannins through the enzymatic hydrolysis of tannase alone, pectinase plus cellulase, or a mixture, in white, red and mixed of grape pomaces, which were obtained from Brazilian wine production. The content of condensed tannins decreased in the enzymatic treatments with respect to the control treatment (without enzymes) and had variations in the different grape pomaces. The best results were obtained in red grape pomace in a treatment with pectinase-cellulase (21.5 mg catechin equivalents (CE)/g DM). The main polyphenolic compounds found were catechin and procyanidin B2, catechin standing out for all treatments, with range of values for catechin and procyanidin being from 575–2009 and 166–1071 mg CE/g DM, respectively. The highest values of these compounds were observed in the grape pomace network, although they were not affected by enzymatic treatments.

In another study, isolation of procyanidins from lychee pericarp by ultra-high-pressure (UHP) extraction was compared to UAE and extraction with ethanol (ECE), to evaluate the polyphenolic profile and antioxidant activity of samples dried in an oven at 80 °C for 36 h. Polyphenolic compounds such as procyanidins A2, procyanidin B2, epicatechin, isoquercitrin and quercetin-3-rutinoside-7-rhamnoside were identified. The B2 procyanidins content was 1.13, 1.21 and 1.29 mg/g in ECE, UAE, UHP, respectively. However, the content of the A2 procyanidin was higher, with values of 4.46, 4.68, 4.97 mg/g in the same extraction treatments. These results were correlated with antioxidant activity tests, where the content of total polyphenols and antioxidant activity increased when UHP was used. Although studies have confirmed the presence of lychee procyanidins, few studies have focuses on the extraction of these compounds. The authors state that the yields of polyphenols could be improved with the adjustment of temperature and pressure in the extraction processes, since compounds such as anthocyanins are sensitive to heat, and in the case of procyanidins they can be polymerized at high temperature and pressure [195].

On the other hand, procyanidin oligomers have been extracted and purified mainly from by-products of the wine industry such as grape seeds. Due to their availability and cost, the extracts have been marketed in the food industry, especially the dietetic and supplementary market. Procyanidin polymers are macromolecules generated in these purification processes, for which extraction methods have been developed that allow their depolymerization and reduction in molecular size as catechins or oligomers. Structural characteristics and antioxidant activity of procyanidins and their derivatives in methodologies with an ultrasound bath and by a probe were evaluated. The conditions of both extraction methods were varied; the first with continuous and degas mode, and the second with 30% and 70% of amplitude in pulsed mode. The analyzes show the presence of 85% of polymeric procyanidins and 2.5% of monomeric and oligomeric flavan-3-ols. Increases in the molecular masses of these compounds were also observed when using an ultrasonic bath in continuous mode. In the MALDI-TOF analyses, type B procyanidins were observed, and the best results of antioxidant activity were obtained in the probe assays at an amplitude of 70% and a procyanidin concentration of 0.01%, while for the assays carried out in the ultrasonic bath antioxidant activity was better at higher concentration of procyanidins. The data obtained on antioxidant activity were positively affected compared

to controls. The authors suggest that the ultrasound method may constitute an effective strategy to modify the structure of polyphenolic compounds in grape seeds, allowing the formation of procyanidin oligomers and polymers with antioxidant activity, that apparently could happen by the breaking of linkages with proteins and/or polysaccharides [189].

Tannin contents were reported by Kim et al. [196] in grape skin and seed ultrasound-assisted extractions using methanol, ethanol and acetone at different concentrations (10%, 70% and 70%, the latter with HCl addition). The highest content of these compounds was observed in seeds extracted with 70% acetone (acidified) at 14.72 mg/g. The identified compounds were monomers and dimers of tannins such as catechin, epicatechin, epigallocatechin, procyanidin B1 and B2, procyanidin B1 being the main compound extracted for all trials. The highest content was found in skin (1076 mg/kg) and seed (1741 mg/kg) using extractions by acetone and methanol at 70%, respectively. The authors indicate that the content of the type of tannin (monomer or dimer) extracted depends on the type of solvent used. In this study, methanol was more efficient for the extraction of condensed tannins as procyanidins (dimers), while molecules of lower molecular weight, such as catechins (monomers), were extracted mainly with acetone and methanol, both at 70%.

There is extensive information on the extraction of polyphenolic compounds from winemaking pomace and marc. However, few works have focused on the use of other sources such as seedless table grape residues for the optimization of extraction parameters such contact time and solid-to-solvent ratio in UAE and MAE using mixtures of water and acidified ethanol. Crupi et al. [197] used water/ethanol/phosphoric acid (70:30:1) as solvents in UAE and MAE to recover phenolic compounds of seedless table grape residues. The main polyphenolic compounds found were procyanidin B1, procyanidin B2, (+)-catechin, peonidin-3-O-glucoside, quercetin-3-O-rutinoside, quercetin-3-O-glucoside, among others.

In processing of cranberry juice (*Vaccinium macrocarpon*), three by-products are obtained skin, seed and flesh, which are called “cranberry pomace”. The use of wastes for procyanidin extraction is an alternative to reduce the costs of blueberry juice production. Researchers have evaluated the adsorption and desorption capacity of procyanidins by using different amberlite resins (XAD-7HP, XAD-761, XAD-16N, XAD-1180, FPX-66) coupled to UAE, to study if this new method is suitable for the separation and concentration of these compounds. The results showed that the adsorption and desorption capacity of procyanidins on the resin were higher with the resin XAD-7HP. The adsorption of procyanidins on the resin was most marked between the times 600 and 800, with a maximum adsorption value of 52.2 mg/g resin. XAD-7HP resin was also used to evaluate the desorption capacity of procyanidins using different solvents (30%, 50%, 70%, 95% ethanol and 70% acetone), where the highest procyanidin desorption value was found with 95% ethanol (>250 mg/g resin), the lowest desorption capacity was found with 30% ethanol and 70% acetone [198].

Procyanidins have also been extracted from cranberry leaves by negative pressure cavitation (NPCE) and its combination with UAE. This technique was called U-NPCE by the authors. The effects of ethanol concentration, ultrasonic power, temperature, extraction time, negative pressure and solid/liquid ratio were evaluated. The authors reveal that there are still no reports indicating a solvent capable of simultaneously extracting all phenolic compounds; however, methanol followed by ethanol is more efficient for this purpose [199]. In this study, ethanol was chosen because it is food grade and was evaluated at concentrations between 40% and 90%, and for ultrasonic power and negative pressure it was evaluated at 0.3–0.4 W/cm² and −0.06 to −0.08 Pa, respectively. Extraction yields of procyanidins, flavonoids and the total content of polyphenols were influenced by ethanol concentration. At 40% and 70% of solvent, the total content of polyphenols and procyanidins had higher values of 300 mg gallic acid equivalents (GAE)/g DM and 200 mg CE/g DM, respectively, which were obtained at a 70% concentration, while for concentrations between 80 and 90%, extraction yields were decreased. For the ultrasonic power parameter, an increase in extraction yields between 0.2 and 0.35 W was observed, and at the latter value the maximum yield of total polyphenols, procyanidins and flavonoids, was obtained. The

temperature and extraction time positively affected the yields of the compounds studied in a range of values from 5 to 15 min, and from 30 to 50 °C. At these ranges, a gradual decrease was observed for the extraction time, while the temperature remained stable. Negative pressure significantly increased the yield of total polyphenols and procyanidins between -0.04 and -0.07 Pa. The same behavior was observed for a solid/liquid ratio between 1:10 and 1:30 g/mL. The variables ethanol concentration, ultrasonic power, and negative pressure were optimized by response surface methodology and evaluation of the bioactivity of the substances evaluated. From these results it was determined that the U-NPCE method was the most suitable for extraction of phenolic compounds such as procyanidins and flavonoids, especially those sensitive to heat, due to its high yield, bioactivity and shorter treatment time [164].

4.2. Microwave-Assisted Extraction

Microwave extraction (MAE) is a technique used for extraction of polyphenols such as condensed tannins and flavonoids. However, studies of procyanidins, catechins, and their structural differences still need to be updated [185,200–206]. MAE use solvents with a high dissipation factor ($\tan \delta$) or high polarity, such as methanol or water [207]. The mechanism consists of the transfer of heat to solvent by frequencies in the range of 300 MHz to 300 GHz, facilitating the disruption of cell wall and cellular structures. The interaction between solvent molecules and compounds released increases by the formation of pores that allow rapid mass transfer resulting in an efficient extraction process [208]. The results depend on factors such as concentration, volume, and chemical characteristics of the solvent and the cell wall [209]. The advantages of this technique are high-quality substance recovery, low use solvent, fewer plant materials, moderate time-extraction and paid energy transfer [173,184,210]. There are reports of other factors, such as extraction temperature, pressure, pH, solvent concentration and particle size, which influence choice of extraction method and solvent. However, the target compounds determine this selection, since the extraction process is specific for each plant material [91,209,211]. The variability of the food matrix and the process variables promote the selection of optimal conditions [212]. Various factors influence on the yield of the substances using this technique include temperature, time, type of solvent, ratio (solvent/solid) and power. Authors suggest response surface methodology (RSM) could reduce experiment size [157,213].

To increase extraction yields, process conditions could be modified. An example is the technique of microwave superheated water extraction (MWE) [210]. Previous findings revealed interactions between nonextractable procyanidin (native and oxidized) and polysaccharides in apple pomace using acetone (60%) and water as solvents with extraction temperatures above 100 °C for 2 and 5 min in each treatment [173]. Previous work was reported in extractions of microwave-assisted seed grape proanthocyanidin yield with recovery rates of 30.7 mg g^{-1} and 99.3%, respectively, compared with traditional extractions. This technique was carried out in two aqueous phases: acetone and ammonium citrate [211]. Proanthocyanidins extraction from apple pulp by MAE was evaluated and could improve yield and reduce extraction times.

The surface response methodology obtains the best extraction yields with the least use of solvent, energy, and time [214,215]. Authors have determined the optimal conditions in extraction processes from residues (bark) of the tree species from *Acacia mollissima*, where condensed tannin concentrations corresponding to 74 mg cyanidin/g bark were achieved using 20% of methanol in water, 182 W and 3.66 min of time exposure [201].

4.3. Supercritical Fluid Extraction

The method of supercritical fluid extraction (SFE), is called supercritical CO₂ extraction (SC-CO₂) when CO₂ is used as a unique solvent [216]. It has potential food applications, roles in pharmaceuticals manufacturing and polymers, and is a potential tool in separation and purification of chemical compounds and natural substances with antioxidant potential [211,214,217]. Some studies have reported results about

flavonoids [218–220], but few are specific for procyanidins from agro-industrial and agroforestry residues [221–223]. This technique cannot be used with a solvent such as n-hexane, chloroform, and dichloromethane. Carbon dioxide can be used with compounds which are easily degradable by temperature, since their critical points of temperature (31 °C), and pressure (74 bar) is low; besides it is inexpensive, possess low viscosity, polarity, and reactivity, is nontoxic, nonexplosive and safe for use in food [224]. CO₂ is useful in nonpolar and slightly polar substance extraction and, in the case of polyphenols other alternatives have been proposed to improve solvation properties and yields, such as CO₂ in mixtures with ethanol (EtOH) and water [225,226]. The process should be designed to take into account that water in supercritical conditions is dangerous [221,225].

Temperatures and pressure monitoring makes the extraction process highly selective, and adjusting these variables obtains bioactive compounds without thermal degradation. Other solvent properties, such as volatility and surface tension are key to produce specificity for each process [227]. Some variables should be taken into account to control processes, including solvent flow rate, temperature, pressure, time, and the features of material [179,228,229]. Another important factor is equipment cost, which affects manufacturing cost. It is crucial to evaluate cost-benefits and extraction yields for future applications [230].

Authors have suggested that SFE is better than traditional methods in compound extractions with biological activity from wastes [231]. In addition, high recovery of compounds from mixtures with solvent extract can involve improved solid/liquid contact through of swelling of the solid sample or semi-solid (matrix), and can involve a low proportion of solvent [107,222]. Other researchers have found that proanthocyanidins were obtained of 139.7, 123.8, 309.3 mg catechin/100 g dried matter for monomeric, oligomeric and polymeric fractions, respectively, with mixtures of pure carbon dioxide, carbon dioxide-water (15%), and water-ethanol (15%) using grape marc at high concentrations, The authors attributed this to antioxidant activity obtained for this treatment (2649.6 mg α -tocopherol/100 g dried matter), which were greater compared to methanol extraction [227]. In a similar study, apple peel was extracted at 50 °C and 25 MPa with a mixture of CO₂-EtOH (25%). This was correlated strongly with antioxidant activity in the presence of catechin, epicatechin, and procyanidin B [231]. Methanol (40%) was used for the modified SFE process. Three steps for the recovery procyanidin monomers were proposed, consisting of a cycle with pure CO₂, followed by a cycle with methanol (40%)-CO₂ and finally with pure methanol. The best recovery rates of catechin (77%) and epicatechin (79%) were achieved in the second step with 60 min of exposure [223]. Other forms of grape pomace extraction, including the coupling of ultrasound techniques with supercritical fluids, has been proposed. The maximum concentrations proanthocyanidins were achieved by SFE, which corresponded to 282.8, 167.4, and 360.3 (mg catechin/100 g dried matter) for monomeric, oligomeric, and polymeric fractions, respectively. Regarding monomeric fractions, the extraction by ultrasound was 10-fold lower than by SFE [232].

4.4. Pressurized Liquid Extraction

Pressurized liquid extraction (PLE), also called as accelerated solvent extraction (ASE), is considered a clean and green technology that generates by-products with added value from different natural sources [124,216,233–235]. However, few studies have been found concerning procyanidin extraction [236], though some works report total flavonoid content [228]. PLE has advantages over conventional extraction, such as the use of short exposure time and low solvent consumption. A range of pressure is employed (4 to 20 MPa) to keep solvent in a liquid state at high temperature when operating conditions are above boiling [219].

This process takes place in a closed and inert system at high temperatures, allowing rapid mass transfer and increasing dissolution of the plant material in the solvent [229]. The molecular interactions into the sample matrix are affected by high temperatures, surface

tension and viscosity of the solvent. Polar substances and thermally sensitive substances have been extracted successfully with water and ethanol. The most common solvent used in PLE is water, being non-toxic, non-inflammable, and having a low cost [237]. According to operating conditions, the procyanidin content may vary. Studies have reported interactions between temperature, pressure, and/or time extraction. Okiyama et al. [29] performed extraction kinetics with cocoa bean shell at 60, 75 and 90 °C for 50 min and using 10.35 MPa. The highest yields of procyanidin were obtained at 90 °C, but this content decreased after 30 min. Researchers deduced possible changes in the matrix-solute. Mustafa and Turner [237] and Wijngaard et al. [238] indicated that the use of PLE did not increase the extraction of bioactive compounds with respect to solid-liquid extraction.

The use of PLE for bioactive substances extraction from Blackberry residues was evaluated using acidified water at 100 °C, which affected negatively the anthocyanin content but promoted the increase of activity antioxidant and total phenolics yield. Authors attributed these results to the possible presence of procyanidins and other compounds; however, the latter compounds were not measured. High temperatures allow the breakdown of interactions (hydrogen bonds, Van der Waals and others), which occur between the solvent and the plant material [234]. This activity also may be a consequence of the generation of Maillard reaction products that could affect procyanidins content. Other changes in nutritional and physicochemical characteristics have been observed [228].

An interesting option is the use of enzymes with PLE to investigate compounds from crude Guarana seeds; a plant with health benefits. This work was achieved to improve concentrations of catechin (50.59 g/100 g extract) and epicatechin (31.32 g/100 g extract) pressurizing the system at 10 MPa. The results were best with treatments using water-ethanol (50% *w/w*) [239], and 20 times higher than a study carried out with SFE using the same plant source [240], possibly due to low affinity of CO₂ by polar molecules such as catechins [239]. Understanding of phenomena occurring in PLE has been mathematically modeled to optimize the process, determine interactions between variables, and allow scale-up [241].

Subcritical Water Extraction

A modification of PLE using only water in extraction system has been reported in the literature. Different names could be found, for example, subcritical water extraction (SWE), superheated water extraction, pressurized low polarity water extraction and pressurized hot water extraction [242], but the mechanism is the same.

This method represents an alternative use of organic solvents and could reduce negative effects to the environment and risks for human health. The use of new solvents is necessary to overcome these limitations [221]. Moreover, unlike traditional methods, it does not require removal proceedings after the process, and manipulation is automated, allowing savings of time and money. It also has good selectivity with rapid extraction. Reports have shown that treatments with SWE have a manufacturing cost higher than assays with supercritical fluids (carbon dioxide) and may be better for total flavonoid content than traditional methods, and nontraditional methods such as UAE and MAE [225,243–245]. SWE is used in different fields to extract bioactive compounds of different polarities, obtained using water as the solvent at high temperatures and pressures [225].

The main property of subcritical water is its dielectric constant (ϵ), which depends on the extraction temperature. By controlling this variable, water polarity can be changed, and thus its solvation capacity. The characteristics of water according to its dielectric constant, facilitates obtaining a wide variety of byproducts.

Other variables such as exposition-time during treatment and chemical composition of plant material represent key points in obtaining target compounds with specific characteristics. The adjustment of temperature and pressure between 100 and 374.1 °C and 1 and 221 bar, can achieve changes in viscosity, surface tension, polarity and diffusivity of water, besides improving sample solubility and mass transfer [235]. In high-temperature

extractions of flavonoids, it was reported that the viscosity, density and surface tension of water can influence the structural characteristics of these compounds. Ko et al. [246] revealed the efficiency of the SWE method in extractions with residues of onion skins and sea-buckthorn leaves for nonpolar flavonoids, where temperature determined the presence of hydrogen bonding in the molecule. In this study flavonoid extractions with hydroxyl groups at low temperatures were achieved.

In previous work with winemaking residues, proanthocyanidins were extracted from grape seeds at different temperatures and cycle extractions using subcritical water. Each treatment resulted in changes in structure, linkages of catechin, and antioxidant activity of the compound. The authors indicated that this strategy allowed selectivity of processes; the type of procyanidin, number of catechin units, and ubication galloylated moieties are influenced by extraction temperature and this variable can be applied individually or sequentially. High temperatures favor polymerization of procyanidins, increased procyanidin trimers and tetramers content occurring at 150 °C, whereas subsequent treatments at 100–150 °C favored procyanidins with galloylated moieties [244].

5. Conclusions

Agro-industrial wastes can be used as renewable sources for the extraction of procyanidins. Undoubtedly, proper selection of the solvent and extraction technique can significantly influence the yields of these compounds. In the case of solvents, those with the highest affinity for procyanidins are methanol, ethanol and acetone, in mixtures with water. The ultrasound technique is the most preferred by researchers, followed by MAE and ASE. In order to improve extraction efficiency and procyanidin yields, UAE has been combined with other methods such as MAE, UNPLE, UHP, and hot water, among others. This is because ultrasonic extraction does not use high temperatures and is environmentally friendly. In addition it could allow greater stability of the biological activity of extracted compounds.

On the other hand, procyanidins are molecules of industrial interest for their biological properties and their effect on human health. It is common to find procyanidin extracts with high antioxidant activity, which may vary according to the plant material and the geographical area of the crop origin. Different types of procyanidins have been identified in agro-industrial wastes, among them A2, B1, B2, B3 and C1. B1 and B2 being the most frequently found.

We are aware that it is necessary to promote the saving of natural resources and promote their efficient use. Therefore, here we have shown the potential of different agro-industrial wastes as cheap sources of procyanidins, among which grape seed, litchi pericarp and plant bark are the most studied sources. In this review it was found that about 90% of studies are focused on the polyphenolic profile and biological activity of different types of wastes, while a small fraction of these studies focussed only on procyanidins. Therefore, this review encourages the researcher to study cheap and easily accessible raw plant materials as sources of procyanidins.

Author Contributions: Conceptualization, L.J.V.-H. and C.N.A.; methodology, L.J.V.-H., J.A.A.-V., J.E.W.-P. and C.N.A.; software, L.J.V.-H. and C.N.A.; validation, L.J.V.-H., J.A.A.-V., J.E.W.-P.; formal analysis, L.J.V.-H.; investigation, L.J.V.-H.; resources, M.L.C.-G., J.E.W.-P., J.C.C.-E. and C.N.A.; data curation, L.J.V.-H., J.A.A.-V., J.E.W.-P. and C.N.A.; writing—original draft preparation, L.J.V.-H.; writing—review and editing, L.J.V.-H., J.A.A.-V., J.E.W.-P., M.L.C.-G., J.C.C.-E. and C.N.A.; visualization, L.J.V.-H. and C.N.A.; supervision, J.A.A.-V. and J.E.W.-P.; M.L.C.-G. and C.N.A.; funding acquisition, C.N.A. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by CONACYT, grant number FOSEC_CB 2017-18 A1-S-42515. The APC was funded by project CONACYT-SEP-CB A1-S-42515.

Acknowledgments: The authors thank National Council of Science and Technology (CONACYT, México) for the financial support given to this project through the program of Basic Science CONACYT-SEP 2017-18 and the national program of scholarship of the PNP-CONACYT through the financial support (CVU 1013484).

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

Abbreviations

UAE, ultrasound-assisted extraction; MAE, microwave-assisted extraction; ASE, accelerated solvent extraction; PLE, pressurized liquid extraction; HE, hot extraction; HR, heat reflux; M, maceration; P, percolation; SSE, successive solvent extraction; SFE, supercritical fluid extraction; SWE, subcritical water extraction; MWE, microwave superheated water extraction; ASE, accelerated solvent extraction; CME, catechin monohydrated equivalents; DE/AE Diethyl ether/ethyl acetate; HIUS, high-intensity ultrasound; FTIR, Fourier transform infrared spectroscopy; CE, catechin equivalents; DM, dry matter; NPCE, negative pressure cavitation extraction; GAE acid equivalents; DP, degree of polymerization; C, catechin; EC, epicatechin; PCs, procyanidins; PCO, oligomeric procyanidins; PCP, polymeric procyanidin; CT, condensed tannins; CME, catechin monohydrated equivalents.

References

1. Smeriglio, A.; Barreca, D.; Bellocchio, E.; Trombetta, D. Proanthocyanidins and Hydrolysable Tannins: Occurrence, Dietary Intake and Pharmacological Effects. *Br. J. Pharmacol.* **2017**, *174*, 1244–1262. [[CrossRef](#)] [[PubMed](#)]
2. Tanase, C.; Coșarcă, S.; Muntean, D.-L. A Critical Review of Phenolic Compounds Extracted from the Bark of Woody Vascular Plants and Their Potential Biological Activity. *Molecules* **2019**, *24*, 1182. [[CrossRef](#)]
3. De Hoyos-Martínez, P.L.; Merle, J.; Labidi, J.; Charrier-El Bouhtoury, F. Tannins Extraction: A Key Point for Their Valorization and Cleaner Production. *J. Clean Prod.* **2019**, *206*, 1138–1155. [[CrossRef](#)]
4. Yang, L.; Wen, K.-S.; Ruan, X.; Zhao, Y.-X.; Wei, F.; Wang, Q. Response of Plant Secondary Metabolites to Environmental Factors. *Molecules* **2018**, *23*, 762. [[CrossRef](#)] [[PubMed](#)]
5. Dai, J.; Mumper, R.J. Plant Phenolics: Extraction, Analysis and Their Antioxidant and Anticancer Properties. *Molecules* **2010**, *15*, 7313–7352. [[CrossRef](#)] [[PubMed](#)]
6. Wang, S.Y.; Camp, M.J.; Ehlenfeldt, M.K. Antioxidant Capacity and α -Glucosidase Inhibitory Activity in Peel and Flesh of Blueberry (*Vaccinium* Spp.) Cultivars. In *Food Chemistry*; Elsevier: Amsterdam, The Netherlands, 2012; Volume 132, pp. 1759–1768. [[CrossRef](#)]
7. Dai, T.; Chen, J.; McClements, D.J.; Li, T.; Liu, C. Investigation the Interaction between Procyanidin Dimer and α -Glucosidase: Spectroscopic Analyses and Molecular Docking Simulation. *Int. J. Biol. Macromol.* **2019**, *130*, 315–322. [[CrossRef](#)] [[PubMed](#)]
8. David, I.M.B.; De Souza Fernandes, F.; Dos Santos Silva Ferreira, J.B.; Lüdtke, D.D.; Martins, D.F.; Bobinski, F.; Da Silva, T.B.G.C.; Buffon, L.D.; Kopper, M.B.R.; Da Silva, G.S.; et al. Dietary Supplementation with Procyanidin-Rich *Pinus Pinaster* Extract Is Associated with Attenuated Ehrlich Tumor Development in Mice. *Nutr. Res.* **2019**, *62*, 41–50. [[CrossRef](#)]
9. Mao, J.T.; Xue, B.; Smoake, J.; Lu, Q.Y.; Park, H.; Henning, S.M.; Burns, W.; Bernabei, A.; Elashoff, D.; Serio, K.J.; et al. MicroRNA-19a/b Mediates Grape Seed Procyanidin Extract-Induced Anti-Neoplastic Effects against Lung Cancer. *J. Nutr. Biochem.* **2016**, *34*, 118–125. [[CrossRef](#)]
10. Yuan, H.; Zhu, X.; Wang, W.; Meng, L.; Chen, D.; Zhang, C. Hypoglycemic and Anti-Inflammatory Effects of Seabuckthorn Seed Protein in Diabetic ICR Mice. *Food Funct.* **2016**, *7*, 1610–1615. [[CrossRef](#)] [[PubMed](#)]
11. Goodrich, K.M.; Smithson, A.T.; Ickes, A.K.; Neilson, A.P. Pan-Colonic Pharmacokinetics of Catechins and Procyanidins in Male Sprague-Dawley Rats. *J. Nutr. Biochem.* **2015**, *26*, 1007–1014. [[CrossRef](#)]
12. Dorenkott, M.R.; Griffin, L.E.; Goodrich, K.M.; Thompson-Witrick, K.A.; Fundaro, G.; Ye, L.; Stevens, J.R.; Ali, M.; O'Keefe, S.F.; Hulver, M.W.; et al. Oligomeric Cocoa Procyanidins Possess Enhanced Bioactivity Compared to Monomeric and Polymeric Cocoa Procyanidins for Preventing the Development of Obesity, Insulin Resistance, and Impaired Glucose Tolerance during High-Fat Feeding. *J. Agric. Food Chem.* **2014**, *62*, 2216–2227. [[CrossRef](#)] [[PubMed](#)]
13. Dahiya, S.; Kumar, A.N.; Shanthi Sraavan, J.; Chatterjee, S.; Sarkar, O.; Mohan, S.V. Food Waste Biorefinery: Sustainable Strategy for Circular Bioeconomy. *Bioresour. Technol.* **2018**, *248*, 2–12. [[CrossRef](#)] [[PubMed](#)]
14. Lin, C.S.K.; Pfaltzgraff, L.A.; Herrero-Davila, L.; Mubofu, E.B.; Abderrahim, S.; Clark, J.H.; Koutinas, A.A.; Kopsahelis, N.; Stamatelatou, K.; Dickson, F.; et al. Food Waste as a Valuable Resource for the Production of Chemicals, Materials and Fuels. Current Situation and Global Perspective. *Energy Environ. Sci.* **2013**, *6*, 426–464. [[CrossRef](#)]
15. Strazzera, G.; Battista, F.; Garcia, N.H.; Frison, N.; Bolzonella, D. Volatile Fatty Acids Production from Food Wastes for Biorefinery Platforms: A Review. *J. Environ. Manage.* **2018**, *226*, 278–288. [[CrossRef](#)] [[PubMed](#)]
16. Billerach, G.; Rouméas, L.; Dubreucq, E.; Fulcrand, H. Furanolysis with Menthofuran: A New Depolymerization Method for Analyzing Condensed Tannins. *J. Agric. Food Chem.* **2020**, *68*, 2917–2926. [[CrossRef](#)] [[PubMed](#)]

17. Wang, L.; Lin, X.; Zhang, J.; Zhang, W.; Hu, X.; Li, W.; Li, C.; Liu, S. Extraction Methods for the Releasing of Bound Phenolics from *Rubus Idaeus* L. Leaves and Seeds. *Ind. Crops Prod.* **2019**, *135*, 1–9. [[CrossRef](#)]
18. Lu, Z.; Jia, Q.; Wang, R.; Wu, X.; Wu, Y.; Huang, C.; Li, Y. Hypoglycemic Activities of A- and B-Type Procyanidin Oligomer-Rich Extracts from Different Cinnamon Barks. *Phytomedicine* **2011**, *18*, 298–302. [[CrossRef](#)]
19. Hümmer, W.; Schreier, P. Analysis of Proanthocyanidins. *Mol. Nutr. Food Res.* **2008**, *52*, 1381–1398. [[CrossRef](#)]
20. Liu, S.X.; White, E. Extraction and Characterization of Proanthocyanidins from Grape Seeds. *Open Food Sci. J.* **2012**, *6*, 5–11. [[CrossRef](#)]
21. Pinelo, M.; Tress, A.G.; Pedersen, M.; Arnous, A.; Meyer, A.S. Effect of Cellulases, Solvent Type and Particle Size Distribution on the Extraction of Chlorogenic Acid and Other Phenols from Spent Coffee Grounds. *Am. J. Food Technol.* **2007**, *2*, 641–651. [[CrossRef](#)]
22. Wang, S.Y.; Yang, L.; Zu, Y.G.; Zhao, C.J.; Sun, X.W.; Zhang, L.; Zhang, Z.H. Design and Performance Evaluation of Ionic-Liquids-Based Microwave-Assisted Environmentally Friendly Extraction Technique for Camptothecin and 10-Hydroxycamptothecin from Samara of *Camptotheca acuminata*. *Ind. Eng. Chem. Res.* **2011**, *50*, 13620–13627. [[CrossRef](#)]
23. Farhat, A.; Ginies, C.; Romdhane, M.; Chemat, F. Eco-Friendly and Cleaner Process for Isolation of Essential Oil Using Microwave Energy. Experimental and Theoretical Study. *J. Chromatogr. A* **2009**, *1216*, 5077–5085. [[CrossRef](#)] [[PubMed](#)]
24. Markom, M.; Hasan, M.; Daud, W.R.W.; Singh, H.; Jahim, J.M. Extraction of Hydrolysable Tannins from *Phyllanthus niruri* Linn.: Effects of Solvents and Extraction Methods. *Sep. Purif. Technol.* **2007**, *52*, 487–496. [[CrossRef](#)]
25. Brown, R.H.; Mueller-Harvey, I.; Zeller, W.E.; Reinhardt, L.; Stringano, E.; Gea, A.; Drake, C.; Ropiak, H.M.; Fryganas, C.; Ramsay, A.; et al. Facile Purification of Milligram to Gram Quantities of Condensed Tannins According to Mean Degree of Polymerization and Flavan-3-Ol Subunit Composition. *J. Agric. Food Chem.* **2017**, *65*, 8072–8082. [[CrossRef](#)] [[PubMed](#)]
26. Enomoto, H.; Nirasawa, T. Localization of Flavan-3-Ol Species in Peanut Testa by Mass Spectrometry Imaging. *Molecules* **2020**, *25*, 2373. [[CrossRef](#)] [[PubMed](#)]
27. Hashim, S.N.N.S.; Boysen, R.I.; Yang, Y.; Schwarz, L.J.; Danylec, B.; Hearn, M.T.W. Parallel Enrichment of Polyphenols and Phytosterols from Pinot Noir Grape Seeds with Molecularly Imprinted Polymers and Analysis by Capillary High-Performance Liquid Chromatography Electrospray Ionisation Tandem Mass Spectrometry. *Talanta* **2020**, *208*, 120397. [[CrossRef](#)] [[PubMed](#)]
28. Li, S.; Yang, Y.; Li, J.; Zhu, Z.; Lorenzo, J.M.; Barba, F.J. Increasing Yield and Antioxidative Performance of Litchi Pericarp Procyanidins in Baked Food by Ultrasound-Assisted Extraction Coupled with Enzymatic Treatment. *Molecules* **2018**, *23*, 2089. [[CrossRef](#)]
29. Okiyama, D.C.G.; Soares, I.D.; Cuevas, M.S.; Crevelin, E.J.; Moraes, L.A.B.; Melo, M.P.; Oliveira, A.L.; Rodrigues, C.E.C. Pressurized Liquid Extraction of Flavanols and Alkaloids from Cocoa Bean Shell Using Ethanol as Solvent. *Food Res. Int.* **2018**, *114*, 20–29. [[CrossRef](#)]
30. Ran, L.; Yang, C.; Xu, M.; Yi, Z.; Ren, D.; Yi, L. Enhanced Aqueous Two-Phase Extraction of Proanthocyanidins from Grape Seeds by Using Ionic Liquids as Adjuvants. *Sep. Purif. Technol.* **2019**, *226*, 154–161. [[CrossRef](#)]
31. Fan, H.; Sun, L.; Yang, L.; Zhou, J.; Yin, P.; Li, K.; Xue, Q.; Li, X.; Liu, Y. Assessment of the Bioactive Phenolic Composition of *Acer truncatum* Seed Coat as a Byproduct of Seed Oil. *Ind. Crops Prod.* **2018**, *118*, 11–19. [[CrossRef](#)]
32. Monrad, J.K.; Suárez, M.; Motilva, M.J.; King, J.W.; Srinivas, K.; Howard, L.R. Extraction of Anthocyanins and Flavan-3-Ols from Red Grape Pomace Continuously by Coupling Hot Water Extraction with a Modified Expeller. *Food Res. Int.* **2014**, *65*, 77–87. [[CrossRef](#)]
33. Meng, Y.; Li, C. Conformational Changes and Functional Properties of Whey Protein Isolate-Polyphenol Complexes Formed by Non-Covalent Interaction. *Food Chem.* **2021**, *364*, 129622. [[CrossRef](#)]
34. Yahya, H.M.; Day, A.; Lawton, C.; Myrissa, K.; Croden, F.; Dye, L.; Williamson, G. Dietary Intake of 20 Polyphenol Subclasses in a Cohort of UK Women. *Eur. J. Nutr.* **2016**, *55*, 1839–1847. [[CrossRef](#)] [[PubMed](#)]
35. Manach, C.; Scalbert, A.; Morand, C.; Rémésy, C.; Jiménez, L. Polyphenols: Food Sources and Bioavailability. *Am. J. Clin. Nutr.* **2004**, *79*, 727–747. [[CrossRef](#)] [[PubMed](#)]
36. Guyot, S.; Le Bourvellec, C.; Marnet, N.; Drilleau, J.F. Procyanidins Are the Most Abundant Polyphenols in Dessert Apples at Maturity. *LWT-Food Sci. Technol.* **2002**, *35*, 289–291. [[CrossRef](#)]
37. Unusan, N. Proanthocyanidins in Grape Seeds: An Updated Review of Their Health Benefits and Potential Uses in the Food Industry. *J. Funct. Foods* **2020**, *67*, 103861. [[CrossRef](#)]
38. Gu, L.; Kelm, M.A.; Hammerstone, J.F.; Beecher, G.; Holden, J.; Haytowitz, D.; Prior, R.L. Screening of Foods Containing Proanthocyanidins and Their Structural Characterization Using LC-MS/MS and Thiolytic Degradation. *J. Agric. Food Chem.* **2003**, *51*, 7513–7521. [[CrossRef](#)] [[PubMed](#)]
39. Tsimogiannis, D.; Oreopoulou, V. Classification of Phenolic Compounds in Plants. In *Polyphenols in Plants*; Elsevier: Amsterdam, The Netherlands, 2019; pp. 263–284. [[CrossRef](#)]
40. Luo, L.; Bai, R.; Zhao, Y.; Li, J.; Wei, Z.; Wang, F.; Sun, B. Protective Effect of Grape Seed Procyanidins against H₂O₂-Induced Oxidative Stress in PC-12 Neuroblastoma Cells: Structure-Activity Relationships. *J. Food. Sci.* **2018**, *83*, 2622–2628. [[CrossRef](#)]
41. Bennick, A. Interaction of Plant Polyphenols with Salivary Proteins. *Crit. Rev. Oral. Biol. Med.* **2002**, *13*, 184–196. [[CrossRef](#)] [[PubMed](#)]

42. Hemingway, R.W.; Karchesy, J.J. Chemistry and Significance of Condensed Tannins. Available online: <https://books.google.es/books?hl=es&lr=&id=7UjUBwAAQBAJ&oi=fnd&pg=PA3&dq=Chemistry+and+Significance+of+Condensed+Tannins.&ots=qz7byY86PZ&sig=DHOk36R4Hfn5j-5NydZ1Hoirj40#v=onepage&q=ChemistryandSignificanceofCondensedTannins.&f=false> (accessed on 12 October 2021).
43. Hemingway, R.W. Structural Variations in Proanthocyanidins and Their Derivatives. In *Chemistry and Significance of Condensed Tannins*; Springer: New York, NY, USA, 1989; pp. 83–107. [\[CrossRef\]](#)
44. Dixon, R.A.; Xie, D.Y.; Sharma, S.B. Proanthocyanidins—A Final Frontier in Flavonoid Research? *New Phytol.* **2005**, *165*, 9–28. [\[CrossRef\]](#) [\[PubMed\]](#)
45. Martins, N.; Ferreira, I.C.F.R. Wastes and By-Products: Upcoming Sources of Carotenoids for Biotechnological Purposes and Health-Related Applications. *Trends Food Sci. Technol.* **2017**, *62*, 33–48. [\[CrossRef\]](#)
46. Ambigaipalan, P.; De Camargo, A.C.; Shahidi, F. Phenolic Compounds of Pomegranate Byproducts (Outer Skin, Mesocarp, Divider Membrane) and Their Antioxidant Activities. *J. Agric. Food Chem.* **2016**, *64*, 6584–6604. [\[CrossRef\]](#)
47. Aron, P.M.; Kennedy, J.A. Flavan-3-Ols: Nature, Occurrence and Biological Activity. *Mol. Nutr. Food Res.* **2008**, *52*, 79–104. [\[CrossRef\]](#) [\[PubMed\]](#)
48. Heim, K.E.; Tagliaferro, A.R.; Bobilya, D.J. Flavonoid Antioxidants: Chemistry, Metabolism and Structure-Activity Relationships. *J. Nutr. Biochem.* **2002**, *13*, 572–584. [\[CrossRef\]](#)
49. Santos-Buelga, C.; Scalbert, A. Proanthocyanidins and Tannin-like Compounds – Nature, Occurrence, Dietary Intake and Effects on Nutrition and Health. *J. Sci. Food Agric.* **2000**, *80*, 1094–1117. [\[CrossRef\]](#)
50. Prior, R.L.; Lazarus, S.A.; Cao, G.; Muccitelli, H.; Hammerstone, J.F. Identification of Procyanidins and Anthocyanins in Blueberries and Cranberries (*Vaccinium* Spp.) Using High-Performance Liquid Chromatography/Mass Spectrometry. *J. Agric. Food Chem.* **2001**, *49*, 1270–1276. [\[CrossRef\]](#) [\[PubMed\]](#)
51. Chen, L.; Yuan, P.; Chen, K.; Jia, Q.; Li, Y. Oxidative Conversion of B- to A-Type Procyanidin Trimer: Evidence for Quinone Methide Mechanism. *Food Chem.* **2014**, *154*, 315–322. [\[CrossRef\]](#)
52. Prior, R.L.; Gu, L. Occurrence and Biological Significance of Proanthocyanidins in the American Diet. *Phytochemistry* **2005**, *66*, 2264–2280. [\[CrossRef\]](#)
53. Home—Eurostat. Available online: <https://ec.europa.eu/eurostat> (accessed on 9 August 2021).
54. Gustavsson, J.; Cederberg, C.; Sonesson, U.; Emanuelsson, A. *The Methodology of the FAO Study: “Global Food Losses and Food Waste-Extent, Causes and Prevention”*; FAO: Rome, Italy, 2011.
55. Arya, S.S.; Venkatram, R.; More, P.R.; Vijayan, P. The Wastes of Coffee Bean Processing for Utilization in Food: A Review. *J. Food Sci. Technol.* **2021**, 1–16. [\[CrossRef\]](#)
56. Cristóbal Garcia, J.; Vila, M.; Giavini, M.; Torres De Matos, C.; Manfredi, S. *Prevention of Waste in the Circular Economy: Analysis of Strategies and Identification of Sustainable Targets—The Food Waste Example*; European Commission: Brussels, Belgium, 2016. [\[CrossRef\]](#)
57. Micanquer-Carlosama, A.; Cortés-Rodríguez, M.; Serna-Cock, L. Formulation of a Fermentation Substrate from Pineapple and Sacha Inchi Wastes to Grow *Weissella cibaria*. *Heliyon* **2020**, *6*, e03790. [\[CrossRef\]](#)
58. Meyve Suyu Endüstrisi Derneği Anasayfa. Available online: <https://meyved.org.tr/> (accessed on 9 August 2021).
59. Home—International Cocoa Organization. Available online: <https://www.icco.org/> (accessed on 9 August 2021).
60. Pascoalino, L.A.; Reis, F.S.; Prieto, M.A.; Barreira, J.C.M.; Ferreira, I.C.F.R.; Barros, L. Valorization of Bio-Residues from the Processing of Main Portuguese Fruit Crops: From Discarded Waste to Health Promoting Compounds. *Molecules* **2021**, *26*, 2624. [\[CrossRef\]](#) [\[PubMed\]](#)
61. Zhu, W.; Li, M.C.; Wang, F.R.; Mackenzie, G.G.; Oteiza, P.I. The Inhibitory Effect of ECG and EGCG Dimeric Procyanidins on Colorectal Cancer Cells Growth Is Associated with Their Actions at Lipid Rafts and the Inhibition of the Epidermal Growth Factor Receptor Signaling. *Biochem. Pharmacol.* **2020**, *175*, 113923. [\[CrossRef\]](#) [\[PubMed\]](#)
62. Li, W.; Liu, J.; Guan, R.; Chen, J.; Yang, D.; Zhao, Z.; Wang, D. Chemical Characterization of Procyanidins from *Spatholobus suberectus* and Their Antioxidative and Anticancer Activities. *J. Funct. Foods* **2015**, *12*, 468–477. [\[CrossRef\]](#)
63. Faria, A.; Calhau, C.; De Freitas, V.; Mateus, N. Procyanidins as Antioxidants and Tumor Cell Growth Modulators. *J. Agric. Food Chem.* **2006**, *54*, 2392–2397. [\[CrossRef\]](#) [\[PubMed\]](#)
64. Jin, A.; Ozga, J.A.; Lopes-Lutz, D.; Schieber, A.; Reinecke, D.M. Characterization of Proanthocyanidins in Pea (*Pisum sativum* L.), Lentil (*Lens culinaris* L.), and Faba Bean (*Vicia faba* L.) Seeds. *Food Res. Int.* **2012**, *46*, 528–535. [\[CrossRef\]](#)
65. Rodríguez-Mateos, A.; Cifuentes-Gomez, T.; Tabatabaee, S.; Lecras, C.; Spencer, J.P.E. Procyanidin, Anthocyanin, and Chlorogenic Acid Contents of Highbush and Lowbush Blueberries. *J. Agric. Food Chem.* **2012**, *60*, 5772–5778. [\[CrossRef\]](#) [\[PubMed\]](#)
66. Usha Rani, M.; Anu Appaiah, K.A. *Gluconacetobacter hansenii* UAC09-Mediated Transformation of Polyphenols and Pectin of Coffee Cherry Husk Extract. *Food Chem.* **2012**, *130*, 243–247. [\[CrossRef\]](#)
67. Sultana, T.; Stecher, G.; Mayer, R.; Trojer, L.; Qureshi, M.N.; Abel, G.; Popp, M.; Bonn, G.K. Quality Assessment and Quantitative Analysis of Flavonoids from Tea Samples of Different Origins by HPLC-DAD-ESI-MS. *J. Agric. Food Chem.* **2008**, *56*, 3444–3453. [\[CrossRef\]](#)
68. Yu, J.; Ahmedna, M.; Goktepe, I.; Dai, J. Peanut Skin Procyanidins: Composition and Antioxidant Activities as Affected by Processing. *J. Food Compos. Anal.* **2006**, *19*, 364–371. [\[CrossRef\]](#)
69. Howell, A.B.; Reed, J.D.; Krueger, C.G.; Winterbottom, R.; Cunningham, D.G.; Leahy, M. A-Type Cranberry Proanthocyanidins and Uropathogenic Bacterial Anti-Adhesion Activity. *Phytochemistry* **2005**, *66*, 2281–2291. [\[CrossRef\]](#)

70. Tomás-Barberán, F.A.; Gil, M.I.; Cremin, P.; Waterhouse, A.L.; Hess-Pierce, B.; Kader, A.A. HPLC–DAD–ESIMS Analysis of Phenolic Compounds in Nectarines, Peaches, and Plums. *J. Agric. Food Chem.* **2001**, *49*, 4748–4760. [[CrossRef](#)]
71. Lachowicz, S.; Oszmiański, J.; Seliga, Ł.; Pluta, S. Phytochemical Composition and Antioxidant Capacity of Seven Saskatoon Berry (*Amelanchier Alnifolia* Nutt.) Genotypes Grown in Poland. *Molecules* **2017**, *22*, 853. [[CrossRef](#)] [[PubMed](#)]
72. Russo, M.; Ronci, M.B.; Vilmercati, A.; Gionfriddo, M.; Fanali, C.; Dugo, L.; Locato, V.; Mondello, L.; De Gara, L. African Baobab (*Adansonia digitata*) Fruit as Promising Source of Procyanidins. *Eur. Food Res. Technol.* **2020**, *246*, 297–306. [[CrossRef](#)]
73. Tembo, D.T.; Holmes, M.J.; Marshall, L.J. Effect of Thermal Treatment and Storage on Bioactive Compounds, Organic Acids and Antioxidant Activity of Baobab Fruit (*Adansonia digitata*) Pulp from Malawi. *J. Food Compos. Anal.* **2017**, *58*, 40–51. [[CrossRef](#)]
74. Miranda-Hernández, A.M.; Muñoz-Márquez, D.B.; Wong-Paz, J.E.; Aguilar-Zárate, P.; De la Rosa-Hernández, M.; Larios-Cruz, R.; Aguilar, C.N. Characterization by HPLC–ESI–MS 2 of Native and Oxidized Procyanidins from Litchi (*Litchi chinensis*) Pericarp. *Food Chem.* **2019**, *291*, 126–131. [[CrossRef](#)] [[PubMed](#)]
75. Wong-Paz, J.E.; Guyot, S.; Aguilar-Zárate, P.; Muñoz-Márquez, D.B.; Contreras-Esquivel, J.C.; Aguilar, C.N. Structural Characterization of Native and Oxidized Procyanidins (Condensed Tannins) from Coffee Pulp (*Coffea Arabica*) Using Phloroglucinolysis and Thioglycolysis-HPLC-ESI-MS. *Food Chem.* **2021**, *340*, 127830. [[CrossRef](#)]
76. Luo, M.; Zhang, R.; Liu, L.; Chi, J.; Huang, F.; Dong, L.; Ma, Q.; Jia, X.; Zhang, M. Preparation, Stability and Antioxidant Capacity of Nano Liposomes Loaded with Procyandins from Lychee Pericarp. *J. Food Eng.* **2020**, *284*, 110065. [[CrossRef](#)]
77. Zhang, S.; Zhang, L.; Wang, L.; Zhao, Y. Total Phenols, Flavonoids, and Procyanidins Levels and Total Antioxidant Activity of Different Korean Pine (*Pinus Koraiensis*) Varieties. *J. For. Res.* **2019**, *30*, 1743–1754. [[CrossRef](#)]
78. Mullen, W.; Nemzer, B.; Stalmach, A.; Ali, S.; Combet, E. Polyphenolic and Hydroxycinnamate Contents of Whole Coffee Fruits from China, India, and Mexico. *J. Agric. Food Chem.* **2013**, *61*, 5298–5309. [[CrossRef](#)] [[PubMed](#)]
79. Bosso, A.; Guaita, M.; Petrozziello, M. Influence of Solvents on the Composition of Condensed Tannins in Grape Pomace Seed Extracts. *Food Chem.* **2016**, *207*, 162–169. [[CrossRef](#)]
80. Li, Q.; Chen, J.; Li, T.; Liu, C.; Liu, W.; Liu, J. Comparison of Bioactivities and Phenolic Composition of *Choerospondias axillaris* Peels and Fleshes. *J. Sci. Food Agric.* **2016**, *96*, 2462–2471. [[CrossRef](#)] [[PubMed](#)]
81. Shrestha, S.S.; Sut, S.; Di Marco, S.B.; Zengin, G.; Gandin, V.; De Franco, M.; Pant, D.R.; Mahomoodally, M.F.; Dall’Acqua, S.; Rajbhandary, S. Phytochemical Fingerprinting and in Vitro Bioassays of the Ethnomedicinal Fern *Tectaria coadunata* (J. Smith) C. Christensen from Central Nepal. *Molecules* **2019**, *24*, 4457. [[CrossRef](#)]
82. Alejo-Armijo, A.; Glibota, N.; Frías, M.P.; Altarejos, J.; Gálvez, A.; Ortega-Morente, E.; Salido, S. Antimicrobial and Antibiofilm Activities of Procyanidins Extracted from Laurel Wood against a Selection of Foodborne Microorganisms. *Int. J. Food Sci. Technol.* **2017**, *52*, 679–686. [[CrossRef](#)]
83. Justino, A.B.; Franco, R.R.; Silva, H.C.G.; Saraiva, A.L.; Sousa, R.M.F.; Espindola, F.S. B Procyanidins of *Annona Crassiflora* Fruit Peel Inhibited Glycation, Lipid Peroxidation and Protein-Bound Carbonyls, with Protective Effects on Glycated Catalase. *Sci. Rep.* **2019**, *9*, 19183. [[CrossRef](#)]
84. Garzón, G.A.; Soto, C.Y.; López-R, M.; Riedl, K.M.; Browmiller, C.R.; Howard, L. Phenolic Profile, in Vitro Antimicrobial Activity and Antioxidant Capacity of *Vaccinium meridionale* Swartz Pomace. *Heliyon* **2020**, *6*, e03845. [[CrossRef](#)]
85. Zhang, L.; Tu, Z.C.; Xie, X.; Wang, H.; Wang, H.; Wang, Z.X.; Sha, X.M.; Lu, Y. Jackfruit (*Artocarpus heterophyllus* Lam.) peel: A better source of antioxidants and α-glucosidase inhibitors than pulp, flake and seed, and phytochemical profile by HPLC-QTOF-MS/MS. *Food Chem.* **2017**, *234*, 303–313. [[CrossRef](#)] [[PubMed](#)]
86. Li, Q.; Liu, C.; Li, T.; McClements, D.J.; Fu, Y.; Liu, J. Comparison of Phytochemical Profiles and Antiproliferative Activities of Different Proanthocyanidins Fractions from *Choerospondias axillaris* Fruit Peels. *Food Res. Int.* **2018**, *113*, 298–308. [[CrossRef](#)] [[PubMed](#)]
87. Rebello, L.P.G.; Ramos, A.M.; Pertuzatti, P.B.; Barcia, M.T.; Castillo-Muñoz, N.; Hermosín-Gutiérrez, I. Flour of Banana (*Musa AAA*) Peel as a Source of Antioxidant Phenolic Compounds. *Food Res. Int.* **2014**, *55*, 397–403. [[CrossRef](#)]
88. Domínguez-Rodríguez, G.; García, M.C.; Plaza, M.; Marina, M.L. Revalorization of Passiflora Species Peels as a Sustainable Source of Antioxidant Phenolic Compounds. *Sci. Total Environ.* **2019**, *696*, 134030. [[CrossRef](#)]
89. Wittenauer, J.; MäcKle, S.; Sußmann, D.; Schweiggert-Weisz, U.; Carle, R. Inhibitory Effects of Polyphenols from Grape Pomace Extract on Collagenase and Elastase Activity. *Fitoterapia* **2015**, *101*, 179–187. [[CrossRef](#)] [[PubMed](#)]
90. Yokozawa, T.; Nakagawa, T. Inhibitory Effects of Luobuma Tea and Its Components against Glucose-Mediated Protein Damage. *Food Chem. Toxicol.* **2004**, *42*, 975–981. [[CrossRef](#)] [[PubMed](#)]
91. De Freitas, M.A.; Andrade, J.C.; Alves, A.I.S.; Dos Santos, F.D.A.G.; Leite-Andrade, M.C.; Sales, D.L.; Nunes, M.; Ribeiro, P.R.V.; Melo Coutinho, H.D.; Morais-Braga, M.F.B.; et al. Use of the Natural Products from the Leaves of the Fruitfull Tree *Persea Americana* against *Candida* Sp. Biofilms Using Acrylic Resin Discs. *Sci. Total Environ.* **2020**, *703*, 134779. [[CrossRef](#)]
92. Kisseih, E.; Lechtenberg, M.; Peteret, F.; Sendker, J.; Zacharski, D.; Brandt, S.; Agyare, C.; Hensel, A. Phytochemical Characterization and in Vitro Wound Healing Activity of Leaf Extracts from *Combretum mucronatum* Schum. & Thonn.: Oligomeric Procyanidins as Strong Inductors of Cellular Differentiation. *J. Ethnopharmacol.* **2015**, *174*, 628–636. [[CrossRef](#)] [[PubMed](#)]
93. Rocchetti, G.; Blasi, F.; Montesano, D.; Ghisoni, S.; Marcotullio, M.C.; Sabatini, S.; Cossignani, L.; Lucini, L. Impact of Conventional/Non-Conventional Extraction Methods on the Untargeted Phenolic Profile of *Moringa oleifera* Leaves. *Food Res. Int.* **2018**, *115*, 319–327. [[CrossRef](#)] [[PubMed](#)]

94. Thiesen, L.C.; Block, L.C.; Zonta, S.L.; Bittencourt, C.M.D.S.; Ferreira, R.A.; Filho, V.C.; Couto, A.G.; Bresolin, T.M.B. Simultaneous Determination of Epicatechin and Procyanidin A2 Markers in *Litchi chinensis* Leaves by High-Performance Liquid Chromatography. *Brazilian J. Pharmacogn.* **2016**, *26*, 168–173. [[CrossRef](#)]
95. Melo, P.S.; Arrivetti, L.D.O.R.; De Alencar, S.M.; Skibsted, L.H. Antioxidative and Prooxidative Effects in Food Lipids and Synergism with α -Tocopherol of Açai Seed Extracts and Grape Rachis Extracts. *Food Chem.* **2016**, *213*, 440–449. [[CrossRef](#)] [[PubMed](#)]
96. Bujor, O.C.; Le Bourvellec, C.; Volf, I.; Popa, V.I.; Dufour, C. Seasonal Variations of the Phenolic Constituents in Bilberry (*Vaccinium myrtillus* L.) Leaves, Stems and Fruits, and Their Antioxidant Activity. *Food Chem.* **2016**, *213*, 58–68. [[CrossRef](#)]
97. Hellenbrand, N.; Sendker, J.; Lechtenberg, M.; Peterreit, F.; Hensel, A. Isolation and Quantification of Oligomeric and Polymeric Procyanidins in Leaves and Flowers of Hawthorn (*Crataegus* Spp.). *Fitoterapia* **2015**, *104*, 14–22. [[CrossRef](#)] [[PubMed](#)]
98. Yan, M.; Chen, M.; Zhou, F.; Cai, D.; Bai, H.; Wang, P.; Lei, H.; Ma, Q. Separation and Analysis of Flavonoid Chemical Constituents in Flowers of *Juglans regia* L. by Ultra-High-Performance Liquid Chromatography-Hybrid Quadrupole Time-of-Flight Mass Spectrometry. *J. Pharm. Biomed. Anal.* **2019**, *164*, 734–741. [[CrossRef](#)]
99. Zeller, W.E.; Ramsay, A.; Ropiak, H.M.; Fryganas, C.; Mueller-Harvey, I.; Brown, R.H.; Drake, C.; Grabber, J.H. ¹H-¹³C HSQC NMR Spectroscopy for Estimating Procyanidin/Prodelphinidin and Cis / Trans -Flavan-3-Ol Ratios of Condensed Tannin Samples: Correlation with Thiolysis. *J. Agric. Food Chem.* **2015**, *63*, 1967–1973. [[CrossRef](#)]
100. Bozan, B.; Tosun, G.; Özcan, D. Study of Polyphenol Content in the Seeds of Red Grape (*Vitis vinifera* L.) Varieties Cultivated in Turkey and Their Antiradical Activity. *Food Chem.* **2008**, *109*, 426–430. [[CrossRef](#)] [[PubMed](#)]
101. Brandão, E.; Fernandes, A.; Guerreiro, C.; Coimbra, M.A.; Mateus, N.; De Freitas, V.; Soares, S. The Effect of Pectic Polysaccharides from Grape Skins on Salivary Protein – Procyanidin Interactions. *Carbohydr. Polym.* **2020**, *236*, 116044. [[CrossRef](#)] [[PubMed](#)]
102. Bräunlich, M.; Slimestad, R.; Wangensteen, H.; Brede, C.; Malterud, K.E.; Barsett, H. Extracts, Anthocyanins and Procyanidins from *Aronia melanocarpa* as Radical Scavengers and Enzyme Inhibitors. *Nutrients* **2013**, *5*, 663–678. [[CrossRef](#)] [[PubMed](#)]
103. Hofmann, T.; Nebehaj, E.; Stefanovits-Bányai, É.; Albert, L. Antioxidant Capacity and Total Phenol Content of Beech (*Fagus sylvatica* L.) Bark Extracts. *Ind. Crops Prod.* **2015**, *77*, 375–381. [[CrossRef](#)]
104. Wei, S.; Chen, H.; Lin, Y. Comparison of Chemical Compositions and Antioxidant Activities of Condensed Tannins from Different Parts of *Calliandra haematocephala*. *J. Wood Chem. Technol.* **2015**, *35*, 193–206. [[CrossRef](#)]
105. Díaz-de-Cerio, E.; Pasini, F.; Verardo, V.; Fernández-Gutiérrez, A.; Segura-Carretero, A.; Caboni, M.F. *Psidium guajava* L. Leaves as Source of Proanthocyanidins: Optimization of the Extraction Method by RSM and Study of the Degree of Polymerization by NP-HPLC-FLD-ESI-MS. *J. Pharm. Biomed. Anal.* **2017**, *133*, 1–7. [[CrossRef](#)]
106. Papillo, V.A.; Locatelli, M.; Travaglia, F.; Bordiga, M.; Garino, C.; Coisson, J.D.; Arlorio, M. Cocoa Hulls Polyphenols Stabilized by Microencapsulation as Functional Ingredient for Bakery Applications. *Food Res. Int.* **2019**, *115*, 511–518. [[CrossRef](#)]
107. Pudziulyte, L.; Jakštas, V.; Ivanauskas, L.; Laukevičienė, A.; Ibe, C.F.D.; Kursvietiene, L.; Bernatoniene, J. Different Extraction Methods for Phenolic and Volatile Compounds Recovery from *Elsholtzia ciliata* Fresh and Dried Herbal Materials. *Ind. Crops Prod.* **2018**, *120*, 286–294. [[CrossRef](#)]
108. Brahem, M.; Renard, C.M.G.C.; Bureau, S.; Watrelot, A.A.; Le Bourvellec, C. Pear Ripeness and Tissue Type Impact Procyanidin-Cell Wall Interactions. *Food Chem.* **2019**, *275*, 754–762. [[CrossRef](#)]
109. Ugartondo, V.; Mitjans, M.; Touriño, S.; Torres, J.L.; Vinardell, M.P. Comparative Antioxidant and Cytotoxic Effect of Procyanidin Fractions from Grape and Pine. *Chem. Res. Toxicol.* **2007**, *20*, 1543–1548. [[CrossRef](#)]
110. Ou, K.; Gu, L. Absorption and Metabolism of Proanthocyanidins. *J. Funct. Foods* **2014**, *7*, 43–53. [[CrossRef](#)]
111. White, B.L.; Howard, L.R.; Prior, R.L. Release of Bound Procyanidins from Cranberry Pomace by Alkaline Hydrolysis. *J. Agric. Food Chem.* **2010**, *58*, 7572–7579. [[CrossRef](#)] [[PubMed](#)]
112. Deprez, S.; Mila, I.; Huneau, J.F.; Tome, D.; Scalbert, A. Transport of Proanthocyanidin Dimer, Trimer, and Polymer across Monolayers of Human Intestinal Epithelial Caco-2 Cells. *Antioxidants Redox Signal.* **2001**, *3*, 957–967. [[CrossRef](#)] [[PubMed](#)]
113. Pietta, P.G. Flavonoids as Antioxidants. *J. Nat. Prod.* **2000**, *63*, 1035–1042. [[CrossRef](#)]
114. Ricardo-da-Silva, J.M.; Cheynier, V.; Souquet, J.-M.; Moutounet, M.; Cabanis, J.-C.; Bourzeix, M. Interaction of Grape Seed Procyanidins with Various Proteins in Relation to Wine Fining. *J. Sci. Food Agric.* **1991**, *57*, 111–125. [[CrossRef](#)]
115. Li, X.; Sui, Y.; Li, S.; Xie, B.; Sun, Z. A-Type Procyanidins from Litchi Pericarp Ameliorate Hyperglycaemia by Regulating Hepatic and Muscle Glucose Metabolism in Streptozotocin (STZ)-Induced Diabetic Mice Fed with High Fat Diet. *J. Funct. Foods* **2016**, *27*, 711–722. [[CrossRef](#)]
116. Arimboor, R.; Arumughan, C. Effect of Polymerization on Antioxidant and Xanthine Oxidase Inhibitory Potential of Sea Buckthorn (*H. rhamnoides*) Proanthocyanidins. *J. Food Sci.* **2012**, *77*, C1036–C1041. [[CrossRef](#)] [[PubMed](#)]
117. Yin, M.; Zhang, P.; Yu, F.; Zhang, Z.; Cai, Q.; Lu, W.; Li, B.; Qin, W.; Cheng, M.; Wang, H.; et al. Grape Seed Procyanidin B2 Ameliorates Hepatic Lipid Metabolism Disorders in Db/Db Mice. *Mol. Med. Rep.* **2017**, *16*, 2844–2850. [[CrossRef](#)] [[PubMed](#)]
118. Kim, Y.; Choi, Y.; Ham, H.; Jeong, H.S.; Lee, J. Protective Effects of Oligomeric and Polymeric Procyanidin Fractions from Defatted Grape Seeds on Tert-Butyl Hydroperoxide-Induced Oxidative Damage in HepG2 Cells. *Food Chem.* **2013**, *137*, 136–141. [[CrossRef](#)]
119. Song, J.H.; Lee, H.J.; Kang, K.S. Procyanidin C1 Activates the Nrf2/HO-1 Signaling Pathway to Prevent Glutamate-Induced Apoptotic HT22 Cell Death. *Int. J. Mol. Sci.* **2019**, *20*, 142. [[CrossRef](#)]
120. López, J.J.; Jardín, I.; Salido, G.M.; Rosado, J.A. Cinnamtannin B-1 as an Antioxidant and Platelet Aggregation Inhibitor. *Life Sci.* **2008**, *82*, 977–982. [[CrossRef](#)]

121. Kruger, M.J.; Davies, N.; Myburgh, K.H.; Lecour, S. Proanthocyanidins, Anthocyanins and Cardiovascular Diseases. *Food Res. Int.* **2014**, *59*, 41–52. [[CrossRef](#)]
122. Chen, L.; Sun, P.; Wang, T.; Chen, K.; Jia, Q.; Wang, H.; Li, Y. Diverse Mechanisms of Antidiabetic Effects of the Different Procyanidin Oligomer Types of Two Different Cinnamon Species on Db/Db Mice. *J. Agric. Food Chem.* **2012**, *60*, 9144–9150. [[CrossRef](#)] [[PubMed](#)]
123. Xiao, Y.; Dong, J.; Yin, Z.; Wu, Q.; Zhou, Y.; Zhou, X. Procyanidin B2 Protects against D-Galactose-Induced Mimetic Aging in Mice: Metabolites and Microbiome Analysis. *Food Chem. Toxicol.* **2018**, *119*, 141–149. [[CrossRef](#)]
124. Corazza, G.O.; Bilibio, D.; Zanella, O.; Nunes, A.L.; Bender, J.P.; Carniel, N.; Dos Santos, P.P.; Priamo, W.L. Pressurized Liquid Extraction of Polyphenols from Goldenberry: Influence on Antioxidant Activity and Chemical Composition. *Food Bioprod. Process.* **2018**, *112*, 63–68. [[CrossRef](#)]
125. Esatbeyoglu, T.; Jaschok-Kentner, B.; Wray, V.; Winterhalter, P. Structure Elucidation of Procyanidin Oligomers by Low-Temperature 1H NMR Spectroscopy. *J. Agric. Food Chem.* **2011**, *59*, 62–69. [[CrossRef](#)] [[PubMed](#)]
126. Justino, A.B.; Miranda, N.C.; Franco, R.R.; Martins, M.M.; Da Silva, N.M.; Espindola, F.S. *Annona muricata* Linn. Leaf as a Source of Antioxidant Compounds with in Vitro Antidiabetic and Inhibitory Potential against α -Amylase, α -Glucosidase, Lipase, Non-Enzymatic Glycation and Lipid Peroxidation. *Biomed. Pharmacother.* **2018**, *100*, 83–92. [[CrossRef](#)] [[PubMed](#)]
127. Spiegler, V.; Liebau, E.; Peppler, C.; Raue, K.; Werne, S.; Strube, C.; Heckendorn, F.; Agyare, C.; Stark, T.; Hofmann, T.; et al. A Hydroalcoholic Extract from *Paullinia pinnata* L. Roots Exerts Anthelmintic Activity against Free-Living and Parasitic Nematodes. *Planta Med.* **2016**, *82*, 1173–1179. [[CrossRef](#)] [[PubMed](#)]
128. Koteswari, L.L.; Kumari, S.; Kumar, A.B.; Malla, R.R. A Comparative Anticancer Study on Procyanidin C1 against Receptor Positive and Receptor Negative Breast Cancer. *Nat. Prod. Res.* **2019**, *34*, 3267–3274. [[CrossRef](#)]
129. Connell, B.J.; Chang, S.Y.; Prakash, E.; Yousfi, R.; Mohan, V.; Posch, W.; Wilflingseder, D.; Moog, C.; Kodama, E.N.; Clayette, P.; et al. A Cinnamon-Derived Procyanidin Compound Displays Anti-HIV-1 Activity by Blocking Heparan Sulfate- and Co-Receptor- Binding Sites on Gp120 and Reverses T Cell Exhaustion via Impeding Tim-3 and PD-1 Upregulation. *PLoS ONE* **2016**, *11*, e0165386. [[CrossRef](#)] [[PubMed](#)]
130. Magoni, C.; Bruni, I.; Guzzetti, L.; Dell’Agli, M.; Sangiovanni, E.; Piazza, S.; Regonesi, M.E.; Maldini, M.; Spezzano, R.; Caruso, D.; et al. Valorizing Coffee Pulp By-Products as Anti-Inflammatory Ingredient of Food Supplements Acting on IL-8 Release. *Food Res. Int.* **2018**, *112*, 129–135. [[CrossRef](#)] [[PubMed](#)]
131. Leonetti, D.; Soleti, R.; Clere, N.; Vergori, L.; Jacques, C.; Duluc, L.; Dourguia, C.; Martínez, M.C.; Andriantsitohaina, R. Extract Enriched in Flavan-3-Ols and Mainly Procyanidin Dimers Improves Metabolic Alterations in a Mouse Model of Obesity-Related Disorders Partially via Estrogen Receptor Alpha. *Front. Pharmacol.* **2018**, *9*, 406. [[CrossRef](#)] [[PubMed](#)]
132. Abdul Karim, A.; Azlan, A.; Ismail, A.; Hashim, P.; Abd Gani, S.S.; Zainudin, B.H.; Abdullah, N.A. Efficacy of Cocoa Pod Extract as Antiwrinkle Gel on Human Skin Surface. *J. Cosmet. Dermatol.* **2016**, *15*, 283–295. [[CrossRef](#)] [[PubMed](#)]
133. Marcinczyk, N.; Jarmoc, D.; Leszczynska, A.; Zakrzeska, A.; Kramkowski, K.; Strawa, J.; Gromotowicz-Poplawska, A.; Chabielska, E.; Tomczyk, M. *Potentilla erecta* Extract Inhibits Arterial Thrombosis in Rat. *Planta Med.* **2016**, *81*, S1–S381. [[CrossRef](#)]
134. Sim, S.Y.J.; Ng, J.W.; Ng, W.K.; Forde, C.G.; Henry, C.J. Plant Polyphenols to Enhance the Nutritional and Sensory Properties of Chocolates. *Food Chem.* **2016**, *200*, 46–54. [[CrossRef](#)]
135. Taparia, S.; Khanna, A. Effect of Procyanidin-Rich Extract from Natural Cocoa Powder on Cellular Viability, Cell Cycle Progression, and Chemoresistance in Human Epithelial Ovarian Carcinoma Cell Lines. *Pharmacogn. Mag.* **2016**, *12*, 109. [[CrossRef](#)]
136. Xiong, J.; Grace, M.H.; Esposito, D.; Wang, F.; Lila, M.A. Phytochemical Characterization and Anti-Inflammatory Properties of *Acacia mearnsii* Leaves. *Nat. Prod. Commun.* **2016**, *11*, 649–653. [[CrossRef](#)]
137. Chai, W.M.; Lin, M.Z.; Feng, H.L.; Zou, Z.R.; Wang, Y.X. Proanthocyanidins Purified from Fruit Pericarp of *Clausena lansium* (Lour.) Skeels as Efficient Tyrosinase Inhibitors: Structure Evaluation, Inhibitory Activity and Molecular Mechanism. *Food Funct.* **2017**, *8*, 1043–1051. [[CrossRef](#)]
138. Chen, L.G.; Chang, C.W.; Tsay, J.G.; Weng, B.B.C. Hepatoprotective Effects of Litchi (*Litchi chinensis*) Procyanidin A2 on Carbon Tetrachloride-Induced Liver Injury in ICR Mice. *Exp. Ther. Med.* **2017**, *13*, 2839–2847. [[CrossRef](#)] [[PubMed](#)]
139. Justino, A.B.; Pereira, M.N.; Peixoto, L.G.; Vilela, D.D.; Caixeta, D.C.; De Souza, A.V.; Teixeira, R.R.; Silva, H.C.G.; De Moura, F.B.R.; Moraes, I.B.; et al. Hepatoprotective Properties of a Polyphenol-Enriched Fraction from *Annona Crassiflora* Mart. Fruit Peel against Diabetes-Induced Oxidative and Nitrosative Stress. *J. Agric. Food Chem.* **2017**, *65*, 4428–4438. [[CrossRef](#)] [[PubMed](#)]
140. Levy, J.; Boyer, R.R.; Neilson, A.P.; O’Keefe, S.F.; Chu, H.S.S.; Williams, R.C.; Dorenkott, M.R.; Goodrich, K.M. Evaluation of Peanut Skin and Grape Seed Extracts to Inhibit Growth of Foodborne Pathogens. *Food Sci. Nutr.* **2017**, *5*, 1130–1138. [[CrossRef](#)] [[PubMed](#)]
141. Neto, J.J.L.; De Almeida, T.S.; De Medeiros, J.L.; Vieira, L.R.; Moreira, T.B.; Maia, A.I.V.; Ribeiro, P.R.V.; De Brito, E.S.; Farias, D.F.; Carvalho, A.F.U. Impact of Bioaccessibility and Bioavailability of Phenolic Compounds in Biological Systems upon the Antioxidant Activity of the Ethanolic Extract of *Triplaris gardneriana* Seeds. *Biomed. Pharmacother.* **2017**, *88*, 999–1007. [[CrossRef](#)]
142. Nocchi, S.R.; Companhoni, M.V.P.; De Mello, J.C.P.; Dias Filho, B.P.; Nakamura, C.V.; Carollo, C.A.; Silva, D.B.; Ueda-Nakamura, T. Antiviral Activity of Crude Hydroethanolic Extract from *Schinus terebinthifolia* against Herpes Simplex Virus Type 1. *Planta Med.* **2017**, *83*, 509–518. [[CrossRef](#)]
143. Li, X.; He, C.; Song, L.; Li, T.; Cui, S.; Zhang, L.; Jia, Y. Antimicrobial Activity and Mechanism of Larch Bark Procyanidins against *Staphylococcus aureus*. *Acta Biochim. Biophys. Sin.* **2017**, *49*, 1058–1066. [[CrossRef](#)] [[PubMed](#)]

144. Aguiar, B.A.A.; Bueno, F.G.; Panizzon, G.; Da Silva, D.B.; Athaydes, B.R.; Gonçalves, R.D.C.R.; Kitagawa, R.R.; Marques, L.L.M.; De Paula, M.N.; Antonelli-Ushirobira, T.M.; et al. Chemical Analysis of the Semipurified Extract of *Paullinia cupana* and Evaluation of in Vitro Inhibitory Effects against *Helicobacter pylori*. *Nat. Prod. Res.* **2018**, *34*, 2332–2335. [[CrossRef](#)]
145. Ameeramja, J.; Perumal, E. Possible Modulatory Effect of Tamarind Seed Coat Extract on Fluoride-Induced Pulmonary Inflammation and Fibrosis in Rats. *Inflammation* **2018**, *41*, 886–895. [[CrossRef](#)] [[PubMed](#)]
146. Chedea, V.S.; Palade, L.M.; Marin, D.E.; Pelmus, R.S.; Habeanu, M.; Rotar, M.C.; Gras, M.A.; Pistol, G.C.; Taranu, I. Intestinal Absorption and Antioxidant Activity of Grape Pomace Polyphenols. *Nutrients* **2018**, *10*, 588. [[CrossRef](#)]
147. Pavlović, J.L.; Mitić, M.; Pavlović, A.N. Variation in the Phenolic Compounds Profile and Antioxidant Activity in Different Parts of Hawthorn (*Crataegus Pentagyna* Willd.) During Harvest Periods OH172057 View Project ON174007 View Project. *Artic. Polish J. Food Nutr. Sci.* **2019**, *69*, 367–378. [[CrossRef](#)]
148. Rodrigues, F.; Moreira, T.; Pinto, D.; Pimentel, F.B.; Costa, A.S.G.; Nunes, M.A.; Gonçalves Albuquerque, T.S.; Costaa, H.; Palmeira-de-Oliveira, A.; Oliveira, A.I.; et al. The Phytochemical and Bioactivity Profiles of Wild *Calluna vulgaris* L. Flowers. *Food Res. Int.* **2018**, *111*, 724–731. [[CrossRef](#)]
149. Martins, N.O.; De Brito, I.M.; Araújo, S.S.O.; Negri, G.; Carlini, E.d.A.; Mendes, F.R. Antioxidant, Anticholinesterase and Antifatigue Effects of *Trichilia catigua* (Catuaba). *BMC Complement. Altern. Med.* **2018**, *18*, 172. [[CrossRef](#)] [[PubMed](#)]
150. Wang, C.M.; Hsu, Y.M.; Jhan, Y.L.; Tsai, S.J.; Lin, S.X.; Su, C.H.; Chou, C.H. Structure Elucidation of Procyanidins Isolated from *Rhododendron formosanum* and Their Anti-Oxidative and Anti-Bacterial Activities. *Molecules* **2015**, *20*, 12787–12803. [[CrossRef](#)] [[PubMed](#)]
151. Aswar, U.M.; Kandhare, A.D.; Mohan, V.; Thakurdesai, P.A. Anti-Allergic Effect of Intranasal Administration of Type-A Procyanidin Polyphenols Based Standardized Extract of Cinnamon Bark in Ovalbumin Sensitized BALB/c Mice. *Phyther. Res.* **2015**, *29*, 423–433. [[CrossRef](#)] [[PubMed](#)]
152. Zou, B.; Xiao, G.; Xu, Y.; Wu, J.; Yu, Y.; Fu, M. Persimmon Vinegar Polyphenols Protect against Hydrogen Peroxide-Induced Cellular Oxidative Stress via Nrf2 Signalling Pathway. *Food Chem.* **2018**, *255*, 23–30. [[CrossRef](#)] [[PubMed](#)]
153. Andrade, C.; Ferreres, F.; Gomes, N.G.M.; Duangrisai, S.; Srisombat, N.; Vajrodaya, S.; Pereira, D.M.; Gil-Izquierdo, A.; Andrade, P.B.; Valentão, P. Phenolic Profiling and Biological Potential of *Ficus Curtipes* Corner Leaves and Stem Bark: 5-Lipoxygenase Inhibition and Interference with NO Levels in LPS-Stimulated RAW 264.7 Macrophages. *Biomolecules* **2019**, *9*, 400. [[CrossRef](#)]
154. Attanzio, A.; D'anneo, A.; Pappalardo, F.; Bonina, F.P.; Livrea, M.A.; Allegra, M.; Tesoriere, L. Phenolic Composition of Hydrophilic Extract of Manna from Sicilian *Fraxinus angustifolia* Vahl and Its Reducing, Antioxidant and Anti-Inflammatory Activity in Vitro. *Antioxidants* **2019**, *8*, 494. [[CrossRef](#)]
155. Chen, H.; Sun, K.; Yang, Z.; Guo, X.; Wei, S. Identification of Antioxidant and Anti- α -Amylase Components in Lotus (*Nelumbo Nucifera*, Gaertn.) Seed Epicarp. *Appl. Biochem. Biotechnol.* **2019**, *187*, 677–690. [[CrossRef](#)] [[PubMed](#)]
156. Feng, J.; Wang, C.; Liu, T.; Li, J.; Wu, L.; Yu, Q.; Li, S.; Zhou, Y.; Zhang, J.; Chen, J.; et al. Procyanidin B2 Inhibits the Activation of Hepatic Stellate Cells and Angiogenesis via the Hedgehog Pathway during Liver Fibrosis. *J. Cell. Mol. Med.* **2019**, *23*, 6479–6493. [[CrossRef](#)]
157. Garrido, T.; Gizdavic-Nikolaidis, M.; Leceta, I.; Urdanpilleta, M.; Guerrero, P.; De la Caba, K.; Kilmartin, P.A. Optimizing the Extraction Process of Natural Antioxidants from Chardonnay Grape Marc Using Microwave-Assisted Extraction. *Waste Manag.* **2019**, *88*, 110–117. [[CrossRef](#)]
158. González De Llano, D.; Liu, H.; Khoo, C.; Moreno-Arribas, M.V.; Bartolomé, B. Some New Findings Regarding the Antiadhesive Activity of Cranberry Phenolic Compounds and Their Microbial-Derived Metabolites against Uropathogenic Bacteria. *J. Agric. Food Chem.* **2019**, *67*, 2166–2174. [[CrossRef](#)]
159. Kamsani, N.E.; Zakaria, Z.A.; Nasir, N.L.M.; Mohtarrudin, N.; Alitheen, N.B.M. Safety Assessment of Methanol Extract of *Melastoma malabathricum* L. Leaves Following the Subacute and Subchronic Oral Consumptions in Rats and Its Cytotoxic Effect against the HT29 Cancer Cell Line. *Evid.-Based Complement. Alternat. Med.* **2019**, *2019*, 5207958. [[CrossRef](#)]
160. Mosbah, H.; Chahdoura, H.; Adouni, K.; Kamoun, J.; Boujbiha, M.A.; Gonzalez-Paramas, A.M.; Santos-Buelga, C.; Ciudad-Mulero, M.; Morales, P.; Fernández-Ruiz, V.; et al. Nutritional Properties, Identification of Phenolic Compounds, and Enzyme Inhibitory Activities of *Feijoa sellowiana* Leaves. *J. Food Biochem.* **2019**, *43*, e13012. [[CrossRef](#)] [[PubMed](#)]
161. Ojeda-Amador, R.M.; Salvador, M.D.; Fregapane, G.; Gómez-Alonso, S. Comprehensive Study of the Phenolic Compound Profile and Antioxidant Activity of Eight Pistachio Cultivars and Their Residual Cakes and Virgin Oils. *J. Agric. Food Chem.* **2019**, *67*, 3583–3594. [[CrossRef](#)]
162. Zeng, L.; Pons-Mercadé, P.; Richard, T.; Krisa, S.; Teissèdre, P.L.; Jourdes, M. Crown Procyanidin Tetramer: A Procyanidin with an Unusual Cyclic Skeleton with a Potent Protective Effect against Amyloid- β -Induced Toxicity. *Molecules* **2019**, *24*, 1915. [[CrossRef](#)]
163. Lohani, U.C.; Muthukumarappan, K. Application of the Pulsed Electric Field to Release Bound Phenolics in Sorghum Flour and Apple Pomace. *Innov. Food Sci. Emerg. Technol.* **2016**, *35*, 29–35. [[CrossRef](#)]
164. Wang, T.; Guo, N.; Wang, S.X.; Kou, P.; Zhao, C.J.; Fu, Y.J. Ultrasound-Negative Pressure Cavitation Extraction of Phenolic Compounds from Blueberry Leaves and Evaluation of Its DPPH Radical Scavenging Activity. *Food Bioprod. Process.* **2018**, *108*, 69–80. [[CrossRef](#)]
165. Li, L.; Zhang, S.; Cui, Y.; Li, Y.; Luo, L.; Zhou, P.; Sun, B. Preparative Separation of Cacao Bean Procyanidins by High-Speed Counter-Current Chromatography. *J. Chromatogr. B Anal. Technol. Biomed. Life Sci.* **2016**, *1036–1037*, 10–19. [[CrossRef](#)]

166. Waterhouse, G.I.N.; Sun-Waterhouse, D.; Su, G.; Zhao, H.; Zhao, M. Spray-Drying of Antioxidant-Rich Blueberry Waste Extracts; Interplay Between Waste Pretreatments and Spray-Drying Process. *Food Bioprocess. Technol.* **2017**, *10*, 1074–1092. [CrossRef]
167. Sun-Waterhouse, D.; Wang, W.; Waterhouse, G.I.N.; Wadhwa, S.S. Utilisation Potential of Feijoa Fruit Wastes as Ingredients for Functional Foods. *Food Bioprocess. Technol.* **2013**, *6*, 3441–3455. [CrossRef]
168. Corrales, M.; Fernandez, A.; Vizoso Pinto, M.G.; Butz, P.; Franz, C.M.A.P.; Schuele, E.; Tauscher, B. Characterization of Phenolic Content, in Vitro Biological Activity, and Pesticide Loads of Extracts from White Grape Skins from Organic and Conventional Cultivars. *Food Chem. Toxicol.* **2010**, *48*, 3471–3476. [CrossRef]
169. Oszmiański, J.; Wojdyło, A.; Kolniak, J. Effect of Pectinase Treatment on Extraction of Antioxidant Phenols from Pomace, for the Production of Puree-Enriched Cloudy Apple Juices. *Food Chem.* **2011**, *127*, 623–631. [CrossRef] [PubMed]
170. Liimatainen, J.; Karonen, M.; Sinkkonen, J. Procyanidin Xylosides from the Bark of *Betula pendula*. *Phytochemistry* **2012**, *76*, 178–183. [CrossRef] [PubMed]
171. Cheng, V.J.; Bekhit, A.E.D.A.; McConnell, M.; Mros, S.; Zhao, J. Effect of Extraction Solvent, Waste Fraction and Grape Variety on the Antimicrobial and Antioxidant Activities of Extracts from Wine Residue from Cool Climate. *Food Chem.* **2012**, *134*, 474–482. [CrossRef]
172. Seabra, I.J.; Dias, A.M.A.; Braga, M.E.M.; De Sousa, H.C. High Pressure Solvent Extraction of Maritime Pine Bark: Study of Fractionation, Solvent Flow Rate and Solvent Composition. *J. Supercrit. Fluids* **2012**, *62*, 135–148. [CrossRef]
173. Fernandes, P.A.R.; Le Bourvellec, C.; Renard, C.M.G.C.; Nunes, F.M.; Bastos, R.; Coelho, E.; Wessel, D.F.; Coimbra, M.A.; Cardoso, S.M. Revisiting the Chemistry of Apple Pomace Polyphenols. *Food Chem.* **2019**, *294*, 9–18. [CrossRef] [PubMed]
174. Mellinas, A.C.; Jiménez, A.; Garrigós, M.C. Optimization of Microwave-Assisted Extraction of Cocoa Bean Shell Waste and Evaluation of Its Antioxidant, Physicochemical and Functional Properties. *LWT* **2020**, *127*, 109361. [CrossRef]
175. Grillo, G.; Boffa, L.; Binello, A.; Mantegna, S.; Cravotto, G.; Chemat, F.; Dizhbite, T.; Lauberte, L.; Telysheva, G. Cocoa Bean Shell Waste Valorisation; Extraction from Lab to Pilot-Scale Cavitation Reactors. *Food Res. Int.* **2019**, *115*, 200–208. [CrossRef]
176. Tamkutė, L.; Liepuoniūtė, R.; Pukalskienė, M.; Venskutonis, P.R. Recovery of Valuable Lipophilic and Polyphenolic Fractions from Cranberry Pomace by Consecutive Supercritical CO₂ and Pressurized Liquid Extraction. *J. Supercrit. Fluids* **2020**, *159*, 104755. [CrossRef]
177. Mason, T.J.; Chemat, F.; Vinatoru, M. The Extraction of Natural Products Using Ultrasound or Microwaves. *Curr. Org. Chem.* **2010**, *15*, 237–247. [CrossRef]
178. Li, W.; Yang, R.; Ying, D.; Yu, J.; Sanguansri, L.; Augustin, M.A. Analysis of Polyphenols in Apple Pomace: A Comparative Study of Different Extraction and Hydrolysis Procedures. *Ind. Crops Prod.* **2020**, *147*, 112250. [CrossRef]
179. Chemat, F.; Zill-E-Huma; Khan, M.K. Applications of Ultrasound in Food Technology: Processing, Preservation and Extraction. In *Ultrasonics Sonochemistry*; Elsevier: Amsterdam, The Netherlands, 2011; Volume 18, pp. 813–835. [CrossRef]
180. Limwachiranon, J.; Huang, H.; Li, L.; Duan, Z.; Luo, Z. Recovery of lotus (*Nelumbo nucifera* Gaertn.) Seedpod flavonoids using polar macroporous resins: The updated understanding on adsorption/desorption mechanisms and the involved intermolecular attractions and bonding. *Food Chem.* **2019**, *299*, 125108. [CrossRef]
181. Milea, A.; Aprodu, I.; Vasile, A.M.; Barbu, V.; Răpeanu, G.; Bahrim, G.E.; Stănciuc, N. Widen the Functionality of Flavonoids from Yellow Onion Skins through Extraction and Microencapsulation in Whey Proteins Hydrolysates and Different Polymers. *J. Food Eng.* **2019**, *251*, 29–35. [CrossRef]
182. Zengin, G.; Cvetanović, A.; Gašić, U.; Stupar, A.; Bulut, G.; Senkardes, I.; Dogan, A.; Sebaluck-Sandoram, R.; Rengasamy, K.R.R.; Sinan, K.I.; et al. Chemical Composition and Bio-Functional Perspectives of *Erica arborea* L. Extracts Obtained by Different Extraction Techniques: Innovative Insights. *Ind. Crop. Prod.* **2019**, *142*, 111843. [CrossRef]
183. Nakajima, V.M.; Madeira, J.V.; Macedo, G.A.; Macedo, J.A. Biotransformation Effects on Anti Lipogenic Activity of Citrus Extracts. *Food Chem.* **2016**, *197*, 1046–1053. [CrossRef] [PubMed]
184. Jing, C.-L.; Dong, X.-F.; Tong, J.-M. Optimization of Ultrasonic-Assisted Extraction of Flavonoid Compounds and Antioxidants from Alfalfa Using Response Surface Method. *Molecules* **2015**, *20*, 15550–15571. [CrossRef] [PubMed]
185. Cheng, X.L.; Wan, J.Y.; Li, P.; Qi, L.W. Ultrasonic/Microwave Assisted Extraction and Diagnostic Ion Filtering Strategy by Liquid Chromatography-Quadrupole Time-of-Flight Mass Spectrometry for Rapid Characterization of Flavonoids in *Spatholobus suberectus*. *J. Chromatogr. A* **2011**, *1218*, 5774–5786. [CrossRef]
186. Novak, I.; Janeiro, P.; Seruga, M.; Oliveira-Brett, A.M. Ultrasound Extracted Flavonoids from Four Varieties of Portuguese Red Grape Skins Determined by Reverse-Phase High-Performance Liquid Chromatography with Electrochemical Detection. *Anal. Chim. Acta* **2008**, *630*, 107–115. [CrossRef]
187. Salarbashi, D.; Dowom, S.A.; Bazzaz, B.S.F.; Khanzadeh, F.; Soheili, V.; Mohammadpour, A. Evaluation, Prediction and Optimization the Ultrasound-assisted Extraction Method Using Response Surface Methodology: Antioxidant and Biological Properties of *Stachys parviflora* L. *Iran. J. Basic Med. Sci.* **2016**, *19*, 829–841. [CrossRef]
188. Ultrasound: Its Chemical, Physical, and Biological Effects. Available online: <https://experts.illinois.edu/en/publications/ultrasound-its-chemical-physical-and-biological-effects> (accessed on 9 August 2021).
189. Muñoz-Labrador, A.; Prodanov, M.; Villamiel, M. Effects of High Intensity Ultrasound on Disaggregation of a Macromolecular Procyanidin-Rich Fraction from *Vitis vinifera* L. Seed Extract and Evaluation of Its Antioxidant Activity. *Ultrason. Sonochem.* **2019**, *50*, 74–81. [CrossRef]

190. Pereira, G.A.; Silva, E.K.; Peixoto Araujo, N.M.; Arruda, H.S.; Meireles, M.A.A.; Pastore, G.M. Obtaining a Novel Mucilage from Mutamba Seeds Exploring Different High-Intensity Ultrasound Process Conditions. *Ultrason. Sonochem.* **2019**, *55*, 332–340. [[CrossRef](#)]
191. Narváez-Flores, M.; Sánchez-Madrigal, M.; Quintero-Ramos, A.; Paredes-Lizárraga, M.A.; González-Laredo, R.F.; Ruiz-Gutiérrez, M.G.; Piñón-Castillo, H.A.; Meléndez-Pizarro, C.O. Ultrasound Assisted Extraction Modeling of Fructans from Agave (*Agave tequilana* Weber Var. azul) at Different Temperatures and Ultrasound Powers. *Food Bioprod. Process.* **2015**, *96*, 232–239. [[CrossRef](#)]
192. Liu, Z.; Yang, L. Antisolvent Precipitation for the Preparation of High Polymeric Procyanidin Nanoparticles under Ultrasonication and Evaluation of Their Antioxidant Activity in Vitro. *Ultrason. Sonochem.* **2018**, *43*, 208–218. [[CrossRef](#)]
193. Ismail, B.B.; Yusuf, H.L.; Pu, Y.; Zhao, H.; Guo, M.; Liu, D. Ultrasound-Assisted Adsorption/Desorption for the Enrichment and Purification of Flavonoids from Baobab (*Adansonia digitata*) Fruit Pulp. *Ultrason. Sonochem.* **2020**, *65*, 104980. [[CrossRef](#)]
194. Yu, Q.; Fan, L.; Li, J. A Novel Process for Asparagus Polyphenols Utilization by Ultrasound Assisted Adsorption and Desorption Using Resins. *Ultrason. Sonochem.* **2020**, *63*, 104920. [[CrossRef](#)] [[PubMed](#)]
195. Zhang, R.; Su, D.; Hou, F.; Liu, L.; Huang, F.; Dong, L.; Deng, Y.; Zhang, Y.; Wei, Z.; Zhang, M. Optimized Ultra-High-Pressure-Assisted Extraction of Procyanidins from Lychee Pericarp Improves the Antioxidant Activity of Extracts. *Biosci. Biotechnol. Biochem.* **2017**, *81*, 1576–1585. [[CrossRef](#)]
196. Kim, H.I.; Hur, Y.Y.; Im, D.J.; Lee, D.H.; Jung, S.M.; Park, S.J.; Kim, S.J. Solvent Extraction Conditions for the Analysis of Condensed Tannins from Grape Skin and Seeds. *Korean J. Food Preserv.* **2019**, *26*, 808–813. [[CrossRef](#)]
197. Crupi, P.; Dipalmo, T.; Clodoveo, M.L.; Toci, A.T.; Coletta, A. Seedless Table Grape Residues as a Source of Polyphenols: Comparison and Optimization of Non-Conventional Extraction Techniques. *Eur. Food Res. Technol.* **2018**, *244*, 1091–1100. [[CrossRef](#)]
198. Gao, C.; Zhao, S.; Yagiz, Y.; Gu, L. Static, Kinetic, and Isotherm Adsorption Performances of Macroporous Adsorbent Resins for Recovery and Enrichment of Bioactive Procyanidins from Cranberry Pomace. *J. Food Sci.* **2018**, *83*, 1249–1257. [[CrossRef](#)] [[PubMed](#)]
199. Mokrani, A.; Madani, K. Effect of Solvent, Time and Temperature on the Extraction of Phenolic Compounds and Antioxidant Capacity of Peach (*Prunus persica* L.) Fruit. *Sep. Purif. Technol.* **2016**, *162*, 68–76. [[CrossRef](#)]
200. Casazza, A.A.; Pettinato, M.; Perego, P. Polyphenols from Apple Skins: A Study on Microwave-Assisted Extraction Optimization and Exhausted Solid Characterization. *Sep. Purif. Technol.* **2020**, *240*, 116640. [[CrossRef](#)]
201. Rhazi, N.; Hannache, H.; Oumam, M.; Sesbou, A.; Charrier, B.; Pizzi, A.; Charrier-El Bouhtoury, F. Green Extraction Process of Tannins Obtained from Moroccan *Acacia mollissima* Barks by Microwave: Modeling and Optimization of the Process Using the Response Surface Methodology RSM. *Arab. J. Chem.* **2019**, *12*, 2668–2684. [[CrossRef](#)]
202. Barrales, F.M.; Silveira, P.; Barbosa, P.D.P.M.; Ruviano, A.R.; Paulino, B.N.; Pastore, G.M.; Macedo, G.A.; Martinez, J. Recovery of Phenolic Compounds from Citrus By-Products Using Pressurized Liquids—An Application to Orange Peel. *Food Bioprod. Process.* **2018**, *112*, 9–21. [[CrossRef](#)]
203. Bujor, O.C.; Ginies, C.; Popa, V.I.; Dufour, C. Phenolic Compounds and Antioxidant Activity of Lingonberry (*Vaccinium vitis-idaea* L.) Leaf, Stem and Fruit at Different Harvest Periods. *Food Chem.* **2018**, *252*, 356–365. [[CrossRef](#)] [[PubMed](#)]
204. Carniel, N.; Dallago, R.M.; Dariva, C.; Bender, J.P.; Nunes, A.L.; Zanella, O.; Bilibio, D.; Luiz Priamo, W. Microwave-Assisted Extraction of Phenolic Acids and Flavonoids from *Physalis angulata*. *J. Food Process Eng.* **2017**, *40*, e12433. [[CrossRef](#)]
205. Xie, J.H.; Dong, C.J.; Nie, S.P.; Li, F.; Wang, Z.J.; Shen, M.Y.; Xie, M.Y. Extraction, Chemical Composition and Antioxidant Activity of Flavonoids from *Cyclocarya paliurus* (Batal.) Iljinskaja Leaves. *Food Chem.* **2015**, *186*, 97–105. [[CrossRef](#)]
206. Sivakumar, V.; Ilanhtiraiyan, S.; Ilayaraja, K.; Ashly, A.; Hariharan, S. Influence of Ultrasound on Avaram Bark (*Cassia auriculata*) Tannin Extraction and Tanning. *Chem. Eng. Res. Des.* **2014**, *92*, 1827–1833. [[CrossRef](#)]
207. Belwal, T.; Bhatt, I.D.; Rawal, R.S.; Pande, V. Microwave-Assisted Extraction (MAE) Conditions Using Polynomial Design for Improving Antioxidant Phytochemicals in *Berberis asiatica* Roxb. Ex DC. Leaves. *Ind. Crops Prod.* **2017**, *95*, 393–403. [[CrossRef](#)]
208. Zhang, J.C.; Wang, C.T.; Wang, C.T.; Wang, S.X.; Sun, B.G. Changes in Components of Aqueous and Non-Aqueous Extracts from Sea Buckthorn Seed Residues through Solid State Fermentation of *Monascus purpureus*. *BioResources* **2019**, *14*, 2197–2215. [[CrossRef](#)]
209. Nayak, B.; Dahmoune, F.; Moussi, K.; Remini, H.; Dairi, S.; Aoun, O.; Khodir, M. Comparison of Microwave, Ultrasound and Accelerated-Assisted Solvent Extraction for Recovery of Polyphenols from Citrus Sinensis Peels. *Food Chem.* **2015**, *187*, 507–516. [[CrossRef](#)] [[PubMed](#)]
210. Coelho, C.; Ribeiro, M.; Cruz, A.C.S.; Domingues, M.R.M.; Coimbra, M.A.; Bunzel, M.; Nunes, F.M. Nature of Phenolic Compounds in Coffee Melanoidins. *J. Agric. Food Chem.* **2014**, *62*, 7843–7853. [[CrossRef](#)]
211. Dang, Y.Y.; Zhang, H.; Xiu, Z.L. Microwave-Assisted Aqueous Two-Phase Extraction of Phenolics from Grape (*Vitis vinifera*) Seed. *J. Chem. Technol. Biotechnol.* **2014**, *89*, 1576–1581. [[CrossRef](#)]
212. Jacotet-Navarro, M.; Rombaut, N.; Deslis, S.; Fabiano-Tixier, A.S.; Pierre, F.X.; Bily, A.; Chemat, F. Towards a “Dry” Bio-Refinery without Solvents or Added Water Using Microwaves and Ultrasound for Total Valorization of Fruit and Vegetable by-Products. *Green Chem.* **2016**, *18*, 3106–3115. [[CrossRef](#)]

213. Vajić, U.J.; Grujić-Milanović, J.; Živković, J.; Šavikin, K.; Godevac, D.; Miloradović, Z.; Bugarski, B.; Mihailović-Stanojević, N. Optimization of Extraction of Stinging Nettle Leaf Phenolic Compounds Using Response Surface Methodology. *Ind. Crops Prod.* **2015**, *74*, 912–917. [[CrossRef](#)]
214. Albuquerque, B.R.; Prieto, M.A.; Barreiro, M.F.; Rodrigues, A.E.; Curran, T.P.; Barros, L.; Ferreira, I.C.F.R. Catechin-Based Extract Optimization Obtained from *Arbutus unedo* L. Fruits Using Maceration/Microwave/Ultrasound Extraction Techniques. *Ind. Crops Prod.* **2017**, *95*, 404–415. [[CrossRef](#)]
215. Li, Y.; Fabiano-Tixier, A.S.; Tomao, V.; Cravotto, G.; Chemat, F. Green Ultrasound-Assisted Extraction of Carotenoids Based on the Bio-Refinery Concept Using Sunflower Oil as an Alternative Solvent. *Ultrason. Sonochem.* **2013**, *20*, 12–18. [[CrossRef](#)] [[PubMed](#)]
216. Wijngaard, H.H.; Ballay, M.; Brunton, N. The Optimisation of Extraction of Antioxidants from Potato Peel by Pressurised Liquids. *Food Chem.* **2011**, *133*, 1123–1130. [[CrossRef](#)]
217. Bordalo, M.; Seabra, I.J.; Silva, A.B.; Terrasso, A.P.; Brito, C.; Serra, M.; Bronze, M.R.; Duarte, C.M.M.; Braga, M.E.M.; De Sousa, H.C.; et al. Using High-Pressure Technology to Develop Antioxidant-Rich Extracts from Bravo de Esmolfe Apple Residues. *Antioxidants* **2021**, *10*, 1469. [[CrossRef](#)] [[PubMed](#)]
218. Krakowska, A.; Rafińska, K.; Walczak, J.; Buszewski, B. Enzyme-assisted optimized supercritical fluid extraction to improve *Medicago sativa* polyphenolics isolation. *Ind. Crops Prod.* **2018**, *124*, 931–940. [[CrossRef](#)]
219. Garcia-Mendoza, M.P.; Paula, J.T.; Paviani, L.C.; Cabral, F.A.; Martinez-Correa, H.A. Extracts from Mango Peel By-Product Obtained by Supercritical CO₂ and Pressurized Solvent Processes. *LWT-Food Sci. Technol.* **2015**, *62*, 131–137. [[CrossRef](#)]
220. Wang, L.; Yang, B.; Du, X.; Yi, C. Optimisation of Supercritical Fluid Extraction of Flavonoids from *Pueraria lobata*. *Food Chem.* **2008**, *108*, 737–741. [[CrossRef](#)] [[PubMed](#)]
221. Abdelmoez, W.; Nage, S.M.; Bastawess, A.; Ihab, A.; Yoshida, H. Subcritical Water Technology for Wheat Straw Hydrolysis to Produce Value Added Products. *J. Clean. Prod.* **2014**, *70*, 68–77. [[CrossRef](#)]
222. Pereira, C.; Meireles, M. Supercritical Fluid Extraction of Bioactive Compounds: Fundamentals, Applications and Economic Perspectives. *Food Bioprocess. Technol.* **2010**, *3*, 340–372. [[CrossRef](#)]
223. Ashraf-Khorassani, M.; Taylor, L.T. Sequential Fractionation of Grape Seeds into Oils, Polyphenols, and Procyanidins via a Single System Employing CO₂-Based Fluids. *J. Agric. Food Chem.* **2004**, *52*, 2440–2444. [[CrossRef](#)]
224. Sánchez-Vicente, Y.; Cabañas, A.; Renuncio, J.A.R.; Pando, C. Supercritical Fluid Extraction of Peach (*Prunus persica*) Seed Oil Using Carbon Dioxide and Ethanol. *J. Supercrit. Fluids* **2009**, *49*, 167–173. [[CrossRef](#)]
225. Todd, R.; Baroutian, S. A Techno-Economic Comparison of Subcritical Water, Supercritical CO₂ and Organic Solvent Extraction of Bioactives from Grape Marc. *J. Clean. Prod.* **2017**, *158*, 349–358. [[CrossRef](#)]
226. Cardenas-Toro, F.P.; Forster-Carneiro, T.; Rostagno, M.A.; Petenate, A.J.; Maugeri Filho, F.; Meireles, M.A.A. Integrated Supercritical Fluid Extraction and Subcritical Water Hydrolysis for the Recovery of Bioactive Compounds from Pressed Palm Fiber. *J. Supercrit. Fluids* **2014**, *93*, 42–48. [[CrossRef](#)]
227. Da Porto, C.; Decorti, D.; Natolino, A. Water and Ethanol as Co-Solvent in Supercritical Fluid Extraction of Proanthocyanidins from Grape Marc: A Comparison and a Proposal. *J. Supercrit. Fluids* **2014**, *87*, 1–8. [[CrossRef](#)]
228. Shang, Y.F.; Kim, S.M.; Um, B.H. Optimisation of Pressurised Liquid Extraction of Antioxidants from Black Bamboo Leaves. *Food Chem.* **2014**, *154*, 164–170. [[CrossRef](#)]
229. Pereira, R.G.; Garcia, V.L.; Nova Rodrigues, M.V.; Martínez, J. Extraction of Lignans from *Phyllanthus amarus* Schum. & Thonn Using Pressurized Liquids and Low Pressure Methods. *Sep. Purif. Technol.* **2016**, *158*, 204–211. [[CrossRef](#)]
230. Veggi, P.C.; Prado, J.M.; Bataglion, G.A.; Eberlin, M.N.; Angela, M.; Meireles, A. The Journal of Supercritical Fluids Obtaining Phenolic Compounds from Jatoba (*Hymenaea courbaril* L.) Bark by Supercritical Fluid Extraction. *J. Supercrit. Fluids* **2014**, *89*, 68–77. [[CrossRef](#)]
231. Massias, A.; Boisard, S.; Baccaunaud, M.; Leal Calderon, F.; Subra-Paternault, P. Recovery of Phenolics from Apple Peels Using CO₂ + Ethanol Extraction: Kinetics and Antioxidant Activity of Extracts. *J. Supercrit. Fluids* **2015**, *98*, 172–182. [[CrossRef](#)]
232. Da Porto, C.; Natolino, A.; Decorti, D. The Combined Extraction of Polyphenols from Grape Marc: Ultrasound Assisted Extraction Followed by Supercritical CO₂ Extraction of Ultrasound-Raffinate. *LWT* **2015**, *61*, 98–104. [[CrossRef](#)]
233. Viganó, J.; Brumer, I.Z.; Braga, P.A.D.C.; Da Silva, J.K.; Maróstica Júnior, M.R.; Reyes Reyes, F.G.; Martínez, J. Pressurized Liquids Extraction as an Alternative Process to Readily Obtain Bioactive Compounds from Passion Fruit Rinds. *Food Bioprod. Process.* **2016**, *100*, 382–390. [[CrossRef](#)]
234. Machado, A.P.D.F.; Pasquel-Reátegui, J.L.; Barbero, G.F.; Martínez, J. Pressurized Liquid Extraction of Bioactive Compounds from Blackberry (*Rubus fruticosus* L.) Residues: A Comparison with Conventional Methods. *Food Res. Int.* **2015**, *77*, 675–683. [[CrossRef](#)]
235. Golmakani, E.; Mohammadi, A.; Ahmadzadeh Sani, T.; Kamali, H. Phenolic and flavonoid content and antioxidants capacity of pressurized liquid extraction and percolation method from roots of *Scutellaria pinnatifida* A. Hamilt. subsp *alpina* (Bornm) Rech. F. *J. Supercrit. Fluids* **2014**, *95*, 318–324. [[CrossRef](#)]
236. Monrad, J.K.; Howard, L.R.; King, J.W.; Srinivas, K.; Mauromoustakos, A. Subcritical Solvent Extraction of Procyanidins from Dried Red Grape Pomace. *J. Agric. Food Chem.* **2010**, *58*, 4014–4021. [[CrossRef](#)] [[PubMed](#)]
237. Mustafa, A.; Turner, C. Pressurized Liquid Extraction as a Green Approach in Food and Herbal Plants Extraction: A Review. *Anal. Chim. Acta* **2011**, *703*, 8–18. [[CrossRef](#)] [[PubMed](#)]
238. Wijngaard, H.; Hossain, M.B.; Rai, D.K.; Brunton, N. Techniques to Extract Bioactive Compounds from Food By-Products of Plant Origin. *Food Res. Int.* **2012**, *46*, 505–513. [[CrossRef](#)]

239. Santana, Á.L.; Queirós, L.D.; Martínez, J.; Macedo, G.A. Pressurized Liquid- and Supercritical Fluid Extraction of Crude and Waste Seeds of Guarana (*Paullinia cupana*): Obtaining of Bioactive Compounds and Mathematical Modeling. *Food Bioprod. Process.* **2019**, *117*, 194–202. [[CrossRef](#)]
240. Marques, L.L.M.; Panizzon, G.P.; Aguiar, B.A.A.; Simionato, A.S.; Cardozo-Filho, L.; Andrade, G.; De Oliveira, A.G.; Guedes, T.A.; De Mello, J.C.P. Guarana (*Paullinia cupana*) Seeds: Selective Supercritical Extraction of Phenolic Compounds. *Food Chem.* **2016**, *212*, 703–711. [[CrossRef](#)]
241. Pereira, D.T.V.; Tarone, A.G.; Cazarin, C.B.B.; Barbero, G.F.; Martínez, J. Pressurized Liquid Extraction of Bioactive Compounds from Grape Marc. *J. Food Eng.* **2019**, *240*, 105–113. [[CrossRef](#)]
242. Pronyk, C.; Mazza, G. Design and Scale-up of Pressurized Fluid Extractors for Food and Bioproducts. *J. Food Eng.* **2009**, *95*, 215–226. [[CrossRef](#)]
243. Cvetanović, A.; Švarc-Gajić, J.; Zeković, Z.; Mašković, P.; Đurović, S.; Zengin, G.; Delerue-Matos, C.; Lozano-Sánchez, J.; Jakišić, A. Chemical and Biological Insights on Aronia Stems Extracts Obtained by Different Extraction Techniques: From Wastes to Functional Products. *J. Supercrit. Fluids* **2017**, *128*, 173–181. [[CrossRef](#)]
244. García-Marino, M.; Rivas-Gonzalo, J.C.; Ibáñez, E.; García-Moreno, C. Recovery of Catechins and Proanthocyanidins from Winery By-Products Using Subcritical Water Extraction. *Anal. Chim. Acta* **2006**, *563*, 44–50. [[CrossRef](#)]
245. Turner, C. Overview of Modern Extraction Techniques for Food and Agricultural Samples. In *Modern Extraction Techniques*; ACS Symposium Series; ACS Publications: Washington, DC, USA, 2006; Volume 926, pp. 3–19. [[CrossRef](#)]
246. Ko, M.J.; Cheigh, C.I.; Chung, M.S. Relationship Analysis between Flavonoids Structure and Subcritical Water Extraction (SWE). *Food Chem.* **2014**, *143*, 147–155. [[CrossRef](#)] [[PubMed](#)]