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Review

Obtaining Value from Wine Wastes: Paving the Way for Sustainable Development

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Abstract: Winemaking is one of the main Portuguese industries and has significantly grown in recent years, thus increasing the quantity of obtained residues. These wastes have a complex chemical composition and structure, and, for this reason, their treatment and valorisation are simultaneously a challenge and an opportunity. After an overview of the wine industry and its wastes, this article intends to review the different solid winemaking wastes, highlighting their chemical composition and structural characteristics, as well as their main potential applications. These wastes, such as grape stalks, can be directly applied as a source of bioenergy in the form of pellets or subjected to chemical/biological processing, resulting in valuable food additives, materials, or chemicals. Grape seeds provide food grade oil with potential biomedical applications. Grape skins are a promising source of biologically active substances. The sugar fraction of grape pomace can be biologically converted to a wide variety of bioproducts, like bioethanol, biogas, polyhydroxyalkanoates, and bacterial cellulose. The integration of the different processes into a biorefinery is also discussed, considering the characteristics of the Portuguese wine industry and pointing out solutions to valorise their wastes.

Keywords: wine processing; wine wastes; polyphenols; bioethanol; grape stalks' pellets; polyhydroxyalkanoates

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1. Introduction: An Overview of the Wine Industry and Its Wastes

The circular economy concept changed the way a process is perceived. The "zero waste" challenge relies on the complete utilisation of feedstocks and on the processing of wastes generated during the transformation process. In this way, wastes can be considered feedstock to obtain several added-value chemicals, fuels, and materials. At the same time, the process costs associated with waste disposal are reduced or eliminated.

Winemaking, one of the oldest food processing technologies, generates a high quantity and variety of wastes. According to the International Organisation of Vine and Wine (OIV), global wine production was estimated to be 2.58 × 108 hL in 2022, with Italy (19.3% of the total production), France (17.7%), Spain (13.8%), the USA (8.7%), and Australia (4.9%) being the top five wine producers [1]. Portugal occupied the 10th place regarding worldwide wine production (2.6%) and the 9th position concerning total vineyard area (2.7%) [1].

Wine production uses grapes as a raw material and is a multistage process, which comprises the cultivation and harvesting of grapes and their transportation and processing for wine production. Wine processing starts with the destemming (stalks' removal) and crushing of grapes [2]. The sequence of the following steps depends on the grapes being red or white, as illustrated in Figure 1. For white wine production, the crushed grapes are pressed for grape pomace removal, and then fermentation occurs, followed by sedimentation/decanting [2,3]. For red wine production, after crushing, the grapes

undergo fermentation and maceration, then pressing (for pomace removal), the completion of maceration, and finally, malolactic fermentation. From this point, the final steps are similar for red and white wine, including sedimentation and decanting, maturation and clarification, stabilisation, and the final step of bottling [4,5].

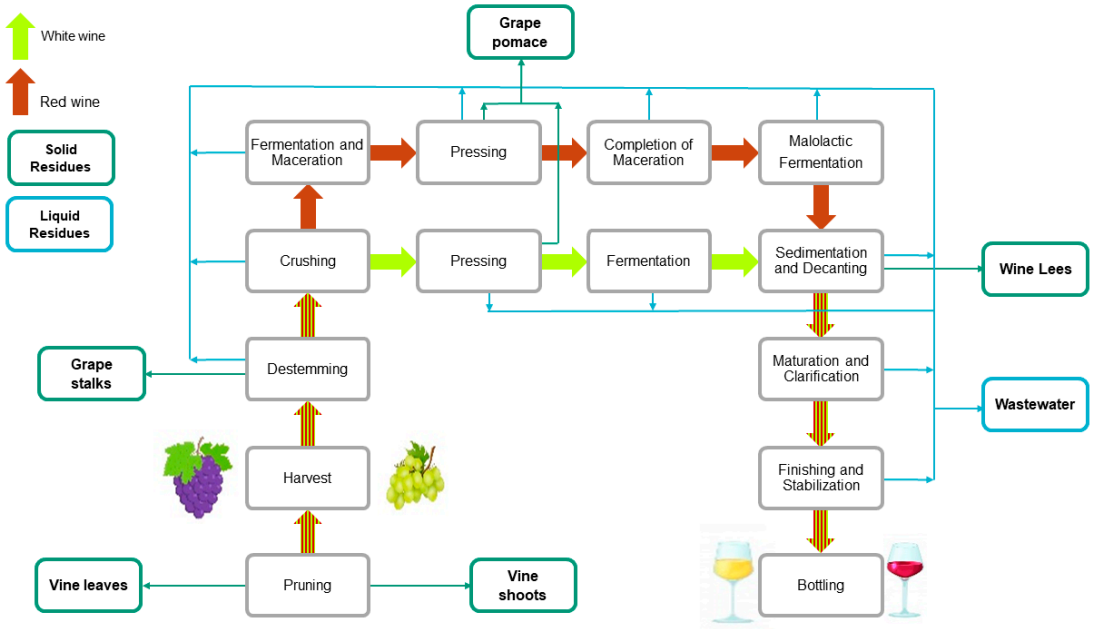

Figure 1. Schematic representation of the red and white wine production steps, including the main generated wastes.

As shown in Figure 1, in wine production, different types of wastes are originated [2,3]. According to Oliveira and Duarte, 1000 kg of harvested grapes generate approximately 750 L of wine and 200 kg of solid waste, which includes grape stalks (30 kg), grape pomace (the solid remains of grape pressing, sometimes also named bagasse or grape marc) (120 kg), wine lees (50 kg), and a variable amount of vine shoots. Furthermore, since winemaking consumes high quantities of water (1–4 L per litre of produced wine), around 1650 L of wastewater are produced [2]. Vine leaves can also be considered a waste from the wine industry. If untreated or not reclaimed, these wastes cause environmental pollution, since they are a source of organic matter with significant levels of phenolic and volatile compounds. For instance, some wastewaters can present biological oxygen demands (BOD) higher than 5 g/L, low pH (<5), and active microbial populations [4]. However, these wastes are not the only contributions to the environmental footprint of winemaking. In fact, the intensive use of soil and the application of pesticides should also be considered [6].

Traditionally, wine wastewaters were submitted to aerobic treatment before being released into water streams [2], and solid wine wastes were landfilled, incinerated, or composted. Until recently, only a small amount of solid waste was used as fertiliser or in animal feed [7]. However, the traditional strategies are strongly discouraged and, in some cases, forbidden by European regulations due to their severe environmental impact [8]. Moreover, liquid and solid wine wastes are rich in molecular compounds with a high added value, namely, phenolic compounds like anthocyanins and flavonols; carbohydrates like glucans, xylans, and mannans; and unsaturated fatty acids, among others [5]. Carbohydrates can be hydrolysed, and the obtained monosaccharides can be converted through microbial processes, for instance, to biofuels (e.g., bioethanol), fatty acids, biopolymers (e.g., polyhydroxyalkanoates (PHAs)), and bacterial cellulose [4,9,10].

Despite winemaking being one of the oldest processes, only in recent years has wine wastes' recovery become a main topic of research. This is illustrated in Figure 2A, where the number of scientific articles published per year containing the words "wine" and

"waste" in the title, abstract, or keywords clearly shows a significant increase since 2005, according to the Web of Science (November 2023) [11]. Before 1990, only eight papers had been published in the previous 20 years. Not surprisingly, most of these publications were authored by researchers from countries with a strong wine industry, with Spain, Italy, China, Brazil, and Portugal being the top five countries, from a total of 87 countries (Figure 2B).

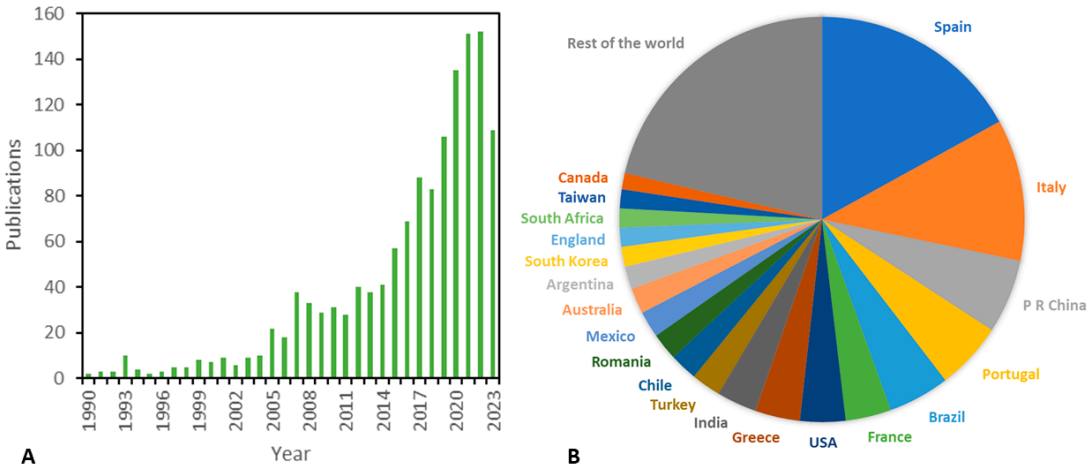

Figure 2. Publications containing "wine" and "waste" as keywords: (**A**) number of articles per year since 1990 and (**B**) distribution of the articles by country (source: Web of Science, November 2023).

The wine industry is one of the most important industries in Portugal, markedly contributing to its economy. In 2016, wine production was the main activity of 910 companies (10% of Portuguese manufacturing companies), representing a turnover of 25% [12]. Most of those companies were small and medium-size enterprises, and 68% of them had been operating for less than 20 years [13]. The valorisation of wine wastes under the biorefinery concept is expected to improve the income of Portuguese wine producers, since the complete utilisation of the raw materials generates less waste to be treated and, at the same time, increases the profit associated with a higher diversity of products.

This work intends to revise the knowledge about the composition and structure of the different solid wastes that can be obtained through the winemaking process with the addition of new, unpublished information. Then, processes that allow for obtaining chemicals (e.g., tannins and lipids), biofuels (e.g., bioethanol), and materials (e.g., PHAs and bacterial cellulose) from solid wine wastes are reviewed. To finalise, a critical analysis of the future perspectives on the field, under the circular economy concept, is presented.

2. Chemical Composition and Structure of Solid Winemaking Wastes

Grape pomace is the major winemaking by-product and is mainly constituted by grape stalks, skins, and seeds [2,14–17]. The production of 100 L of white wine results in 31.2 kg of by-products, including 17 kg of skins and 4 kg of stalks. Slightly lower amounts of waste, about 25 kg of by-products, with the major part also being skins (ca. 13.2 kg) and stalks (ca. 4 kg), are released in the production of 100 L of red wine [14]. The weight ratio of grape seeds and stalks in red and white grape pomaces is about the same [15,17]. The increased interest in the chemical composition and structure of winemaking by-products is due to the need for their disposal and to the uniqueness of some individual compounds with high potential for application in the food industry, biomedicine, and different technical areas, or even as a source of energy [16–18]. The chemical composition of three major grape pomace counterparts is quite different according to the various physiological roles inherent to each component. In this section, the basic information about the general chemical composition and structure of the main components of winemaking by-products is summarised.

2.1. Composition and Structure of Grape Pomace Constituents

2.1.1. Grape Stalks

Grape stalks are fibrous materials whose main function is to provide mechanical support to grapes. Therefore, it is not surprising that the main components of grape stalks are cellulosic fibres [19–24]. Accordingly, the main grape stalks' constituents are cellulose (25–40 wt.%), hemicelluloses (14–25 wt.%), and lignin (17–35 wt.%). It is worth noting that the quantification of the cell wall components in grape stalks provides quite diverse results due to the huge varieties of grape plants, the climatic and regional diversity of their growth, and the chemical methods involved in the analyses [20,23,25]. The average chemical composition of grape stalks from red wine production is presented in Table 1.

Table 1. Chemical composition of grape stalks from red and white grape pomaces.

Composition	Content (wt.%)	
	Red Grape Stalks [23]	**White Grape Stalks ***
Ash	7.0	5.2
Cellulose	30.3	33.1
Proteins	6.1	10.8
Tannins	15.9	8.6
Lignin (Klason)	17.4	17.0
Hemicelluloses	21.0	22.4
Extractives obtained with		
Acetone	2.3	2.9
Dichloromethane	1.0	1.9
Hot water	23.7	-

* unpublished results.

The characteristic feature of grape stalks is a relatively high content of ash, proteins, tannins, and hot water extractives. This fact hinders the correct determination of cell wall components and must be considered while defining the analytical strategies [23]. In addition, the presence of these substances can limit some applications of grape stalks due to their specific behaviour during processing or due to the originated properties of some products produced therein. Salts of potassium and calcium predominate among the ash components [23].

Cellulose, the main component of grape stalks, is a typical polymorph of cellulose I with an average crystallite width of 4.2 nm and a relatively high degree of crystallinity (about 75–76%) [23]. According to this indicator, it is similar to or just slightly inferior to cotton. Xylan is the second polysaccharide in abundance, contributing to ca. 12–15% of grape stalks [23,26]. The heteroxylan of grape stalks possesses a moderate molecular weight (M_w = 19 kDa), is partially acetylated (degree of substitution (DS) = 0.49), and reveals a quite low substitution of the main backbone composed by β-(1,4)-linked D-xylopyranosyl units with α-(1,2)-linked 4-*O*-methyl-α-D-glucuronosyl residues (MeGlc*p*A) (molar ratio 25:1) [26]. The mixed β-(1,3;1,4)-D-glucan, with a molar ratio of β-(1,3)-linked glucopyranosyl units to β-(1,4)-linked glucopyranosyl units of 1:2, was considered the second most abundant structural hemicellulose (2–4 wt.%) after xylan.

One of the features of red grape stalks is the same content of lignin and tannins (hydrolysed and condensed tannins), which distinguishes them from white grape stalks, containing much fewer tannins and a higher proteins content (Table 1). The lignin is essentially constituted by syringyl units (S, 71 mol.%), with a moderate proportion of guaiacyl units (G, 26 mol.%) and a low abundance of *p*-hydroxyphenyl units (H, 3 mol.%) [27]. It is characterised by a relatively low content of β-*O*-4′ structures (39 mol.%); a moderate amount (3–6 mol.%) of β-1′, β-5′ and β-β′ structures; and ca. 20 mol.% of condensed structures of alkyl–aryl and aryl–aryl types. It was proposed that grape stalks' lignin is structurally associated with tannins. The latter easily reacts with lignin, under either

alkaline or acidic conditions, forming condensed structures, thus making the effective delignification of grape stalks by organosolv or kraft cooking impossible [21–23]. Accordingly, the recalcitrance to chemical processing is one of the specific features of grape stalks. The bioprocessing of grape stalks is also hampered by the low accessibility of polysaccharides in the lignin matrix, in combination with polyphenolic substances.

It is noteworthy that hydrolysable tannins predominate over condensed tannins in grape stalks, which are of the procyanidin and prodelphinidin types, the former being predominant [21–23,28]. While hydrolysable tannins are soluble in hot water and hydroalcoholic solutions, condensed tannins can only be extensively removed under alkaline conditions. Among the hydrolysable tannins, quercetin 3-glucuronide is the most abundant, followed by caffeoyltartaric acid and dihydroquercetin 3-rhamnoside (astilbin) [28]. It has been suggested that condensed tannins in stalks are qualitatively intermediate between the seed and skin but cannot be differentiated between red and white varieties.

2.1.2. Grape Skins

Grape skins ensure overall grape integrity, while also being the major winemaking waste. The chemical composition of skins reveals essentially non-structural compounds (sugars, tannins, flavonols, extractives, etc.) from different morphological parts, and limited information is available about the structure of the macromolecular components [29,30]. The diversity of data on the chemical composition of grape skins is even greater than that mentioned for grape stalks. The reason for this is also the huge variety of grape plants, the different climatic conditions of growth, winemaking practices, and the chemical methods involved in the analyses. In particular, a big difference in the chemical composition is found between red and white grape skins due to the different winemaking approaches involved in the production of red and white wines [18,31–33].

The differences in the general composition of red and white skins from typical varieties of the Dão region (Portugal) are presented in Table 2. There is a higher content of cellulose, hemicelluloses, tannins, and proteins in the skins of red grapes than in the skins of white grapes. In contrast, the quantity of water-soluble sugars (mainly glucose and sucrose) and polysaccharides is higher in white grapes than in red grape skins (Table 2). Similar differences were reported for a series of varieties of red and white grape skins from various regions of the USA [31–33] and France [34]. The high quantity of available sugars makes the bioprocessing of white grape skins particularly attractive for different added-value products [30].

Table 2. General chemical composition of red and white grape skins [30,33].

Composition	Abundance (wt.%)	
	Red Grape Skins	White Grape Skins
Ash	7.8	18.3
Cellulose	20.8	18.5
Proteins	18.8	6.7
Tannins	13.8	3.4
Hemicelluloses	12.5	9.0
Extractives obtained with		
Hexane	-	1.3
Dichloromethane	2.9	2.4
Hot water	24.6	48.0

Cellulose is commonly reported in the composition of dietary fibres [31–33] or just as a structural glucan [18–34], without specification of its structural features. Meanwhile, the physical structure of cellulose differs between red and white grape varieties. It was demonstrated that although no significant difference was found between the crystallite widths in the elementary cellulose fibres of red (3.7 nm) and white (3.8 nm) grape skins, the difference

in their degree of crystallinity was quite significant (ca. 66% and 73%, respectively) [29–33]. Among the structural hemicelluloses, xylan is predominant both in red and white grape skins [18,29–31,34]. According to preliminary structural analysis, the xylan in grape skins is a typical partially acetylated heteroxylan [29]. The structural association of the xylan and cuticle components in grape skins was suggested. Among water-soluble polysaccharides, pectin and partially acetylated glucomannan are the most abundant [30,31]. The major pectin polysaccharides identified in grape skins are homogalacturonan conjugated with rhamnogalacturonan I and rhamnogalacturonan II [17]. Most commonly, the acid-insoluble residue of the grape skin, mainly consisting of cuticle material and tannins, is erroneously determined to be lignin. However, it was undeniably proven that grape skins do not contain lignin [29]. Structural polysaccharides in grape skins are embedded in the cutin matrix, which hinders their chemical processing and bioprocessing.

Being a major part of the cuticle, cutin is another important macromolecular component of grape skins [35,36]. Cutin is poorly soluble in most organic solvents, and its long-chain constituents are cross-polymerised with lipid membranes. Cutin contributes to ca. 15 wt.% of grape matter, and its structure is similar to suberin [29,30,33]. It has been suggested that a major part of cuticular waxes is composed of esters of hexadecanoic (palmitic) or octadecanoic (stearic) acids and higher alcohols, primarily hexacosanol, octacosanol, tetracosanol, and triacosanol. The cuticle matter is composed of polyesters that involve hydroxyacids (primarily 7,8-dihydroxy-hexadecanoic and 9,10-dihydroxyoctadecanoic acids) and higher alcohols. The major contribution of hydroxy acids involved in the cutin structure of red grape skins was by 9,10-dihydroxy-octadecanedioic acid (phloionic acid), whereas 9,10,18-trihydroxy-octadecanedioic was the most abundant hydroxy acid in cutin's structure of white grape skins [29]. The relative proportions of different classes of extractives found in dichloromethane in red and white grape skins are summarised in Figure 3. Among triterpenoids, the major fraction, oleanolic acid, and β-sitosterol were the most abundant. Concerning fatty acids, the most abundant were hexacosanoic (ceric), 9,12-octadecadienoic (linoleic), and 9-octadecanoic (oleic) acids. Among the fatty alcohols, 1-hexacosanol and 1-octacosanol predominated. Oleanolic acid occupies nearly 80 wt.% of all extractives in dichloromethane and has high potential in biomedical applications [29,37]. The cutin fraction from grape skins was recently applied for the modification of rayon fibres [38].

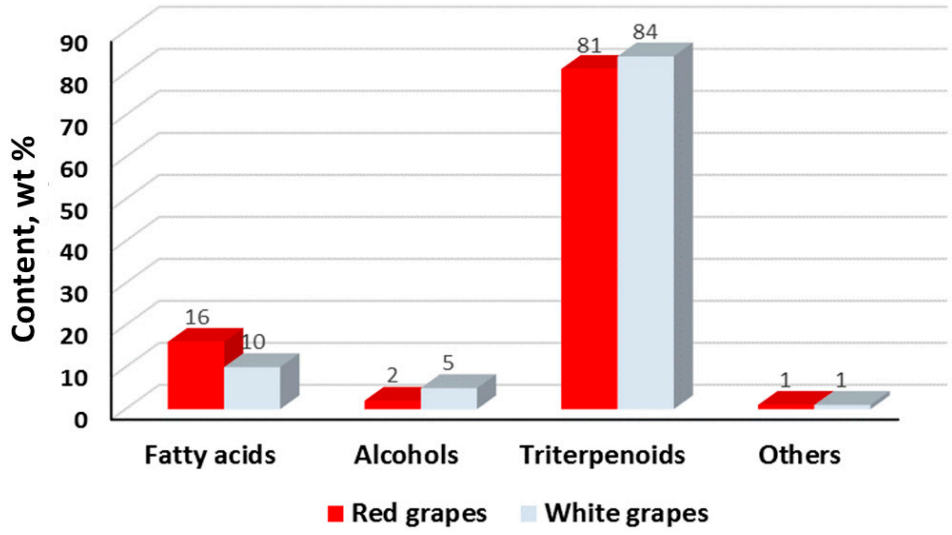

Figure 3. The weight content of the major families of compounds identified in dichloromethane extract from red and white grape skins [29].

Grape skins, especially from red grapes, are particularly rich in polyphenolic compounds (Table 2). In fact, the skins from red grapes commonly contain much higher amounts

of all types of polyphenols (tannins) than the skins from white grapes [31,33,39,40]. At the same time, the variation in tannins' composition is quite significant and strongly depends not only on the grape variety but also on its degree of maturation [41] and the peculiarities of grape processing during wine production [42]. Among the major groups of tannins (Figure 4), procyanidins are the most abundant in both red and white grape skins, followed by flavonoids and anthocyanins [18,31,39,40]. The high amounts of residual tannins in grape skins, especially from red grapes, make them an attractive source of polyphenolics for food applications [43] and other technical applications [22,34].

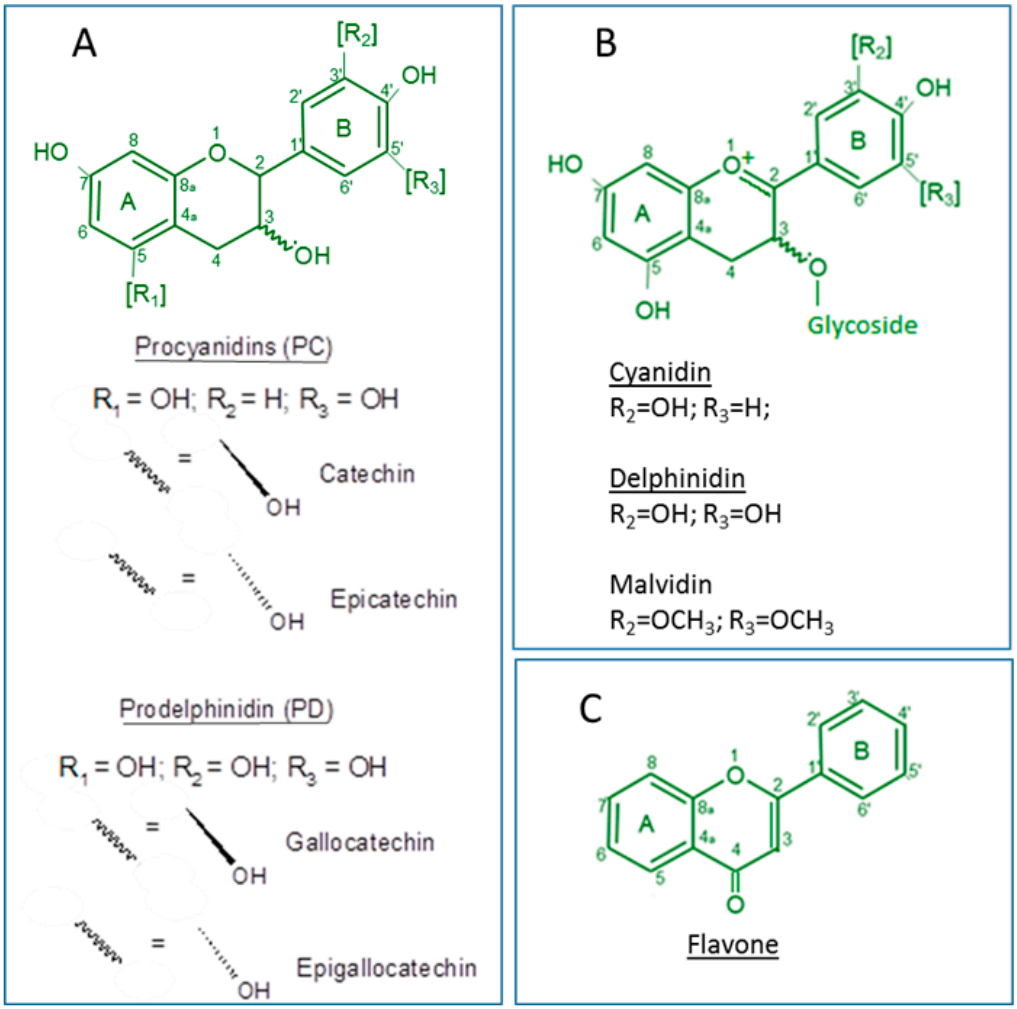

Figure 4. Schematic representation of major groups of tannins present in grape skins: (**A**) basic building blocks of oligomeric procyanidins/prodelphinidins, (**B**) anthocyanins, and (**C**) the basic structure of the flavone backbone, one base molecule of the common families of flavonoids.

2.1.3. Grape Seeds

The diversity of the chemical composition of grape seeds is due to the reasons mentioned above for grape stalks and skins. However, a special feature of the chemical composition of grape seeds is a rather high content of vegetable fats, known as grape seed oil (8–20 wt.%) [15,44]. Among other grape seed components, cellulose is the most abundant, followed by lignin, proteins, tannins, and mineral compounds (Table 3). Moreover, there was no significant difference found between the chemical composition of seeds from red and white grapes [44].

Table 3. General chemical composition of grape seeds [17,44–47].

Composition	Content (wt.%)
Ash	2–4
Cellulose	10–30
Lignin	10–20
Proteins	4–9
Tannins	4–6
Hemicelluloses	3–6
Extractives obtained with	
Hexane	8–20
Hot water	5–10

In general, despite numerous exploratory studies on the use of grape seed residues within the biorefinery context, basic knowledge about its main macromolecular components is quite scarce. Thus, it is reported that the cellulose of grape seeds is a common cellulose I polymorph with a moderate degree of crystallinity [48]. The lignin of grape seeds has only been studied in general terms [45–49]. However, it was suggested that it might be essentially of the guaiacyl (G) type, with a small proportion of p-hydroxyphenyl (H) structures and minor quantities of syringyl (S) units [45]. Semi-quantitative analysis suggests the predominance of β-*O*-4′ structures (ca. 34 mol.%), and a moderate amount (6–10 mol.%) of phenyl coumaran (β-5′) and pinoresinol (β-β′) structures. It was also proposed that grape seeds' lignin is structurally associated with tannins and polysaccharides. Grape seeds' lignin seems also to be bound to proteins during its isolation, thus explaining an apparent increased molecular weight (ca. 10.0 kDa) [48]. According to data from sugars' analysis, the most water-soluble polysaccharide is pectin, and the most abundant structural hemicellulose must be xylan [44,45].

The extractable fatty matter of grape seeds is commonly known as seed oil and was studied in more detail due to its important practical applications in the food industry and biomedicine [50–52]. Seed oil can be obtained by cold pressing, by extraction with non-polar organic solvents (e.g., with hexane providing the highest yield), or by using supercritical extraction with CO_2 [7]. Grape seed oil (GSO) is conditionally subdivided into hydrophilic and lipophilic constituents. Lipophilic substances are mainly unsaturated fatty acids, phytosterols, and tocopherols, while hydrophilic compounds are mainly phenols. Among unsaturated fatty acids, linoleic acid (58–78 wt.%) predominates in GSO [15,47], and oleic (12–28 wt.%) and palmitic (5.5–11.0 wt.%) acids are the second and third in abundance, respectively. The stearic acid content generally does not exceed 3–7 wt.% of the total fatty acids in GSO. Among the fatty acids of minor abundance (0.2–0.5 wt.%), lauric (C12:0), arachidic (C20:0), and palmitoleic (C16:1) acids can be mentioned.

Tocopherols (α-, β-, γ-, and δ-isomers) and tocotrienols (unsaturated forms of tocopherols) are another group of lipophilic constituents of GSO, contributing up to 0.015% [17,44–46]. The most abundant in seeds, from both red and white grapes, is α-tocopherol [17]. Phytosterols (ca. 0.01 wt.%) are also present in GSO, the most abundant being β-sitosterol, followed by stigmasterol and campesterol. Among other classes of extractives, carotenoids [47] and volatile organic compounds such as higher aldehydes (e.g., pentanal, hexanal, 2-hexenal, etc.) and terpenes (e.g., α-pinene and limonene) have also been detected [53]. Grape seeds owe their characteristic smell to these compounds. Among the phospholipids present in GSO, phosphatidylinositol and phosphatidic acid are the most abundant [44].

Phenols constitute a very important group of hydrophilic compounds of GSO, although present in relatively low amounts (20–60 mg gallic acid equivalent (GAE)/kg) [52]. The relatively low concentrations of phenols in GSO may be attributed to their limited liposolubility, because the quantity of polyphenols reported in grape seeds is quite significant (up to ca. 20,000 mg GAE/kg) [54]. The main phenolic compounds found in grape seeds

are flavonoids, especially flavan-3-ols (catechin, epicatechin, and epicatechin 3-*O*-gallate monomers) and their polymers [55,56].

2.2. Vine Shoots

Vine shoots result from the pruning of grape vines being a residue of grape cultivation and not a waste from winemaking. This waste is a lignocellulosic material composed of cellulose, hemicellulose, and lignin. Vine shoots can be delignified, after chemical or enzymatic pretreatments, and then cellulose and hemicellulose can be hydrolysed to obtain sugar solutions, which, in turn, can be converted into several added-value compounds [57]. The hemicelluloses in vine shoots are mainly xylans, mannans, and glucans, so the obtained sugar solutions contain xylose, mannose, and glucose in minor amounts [58]. This waste was already tested in several applications, namely, in pulping, in energy production, in extraction of organic chemical products; in biosurfactants; as a source of antioxidants, antimicrobials, antifeedants, phytotoxic compounds, fungicides, and nutraceuticals; as a source of nutrients for ruminants; as an enological additive in winemaking; as a viticultural biostimulant and as a precursor to optimie sensory features in white wine [59].

2.3. Vine Leaves

Vine leaves are a significant leftover of the wine production process and contain several compounds with potential economic interest. Although scarce, studies on the valorisation of *V. vinifera* leaves showed that ethanolic extracts are rich in phenolic compounds with biological activity (mainly hydroxycinnamic acid derivatives) and that quercetinglycosides and chloroform extracts contain several triterpenoids (e.g., β-amyrin, lupeol, taraxerol, α-tocopherol, and β-sitosterol) [50,60].

2.4. Wine Lees

Wine lees are the solid residue formed after fermentation, during storage, and as a result of the filtration or centrifugation of wine [61]. Despite depending on wine processing, wine lees mainly contain ethanol, tartaric acid, polyphenols, and yeast cells and are usually used as a source of tartaric acid and ethanol [62]. This residue is usually acidic, with a pH between 3 and 6; has a high amount of organic matter; and corresponds to 2–6% (v/v) of produced wine [35]. The presence of yeast cells contributes to a higher amount of nitrogen when compared to other wine wastes. The presence of enzymes hydrolyses polyphenols into smaller phenolic compounds, like gallic or ellagic acids [63].

3. Products from Solid Winemaking Wastes

Due to the complexity and diverse composition of solid wine wastes, more than one product can be obtained by sequential processing. Usually, one or more pretreatment steps are required, and, as a result, some of the desired compounds can be obtained when fractioning the raw material. For example, to obtain the sugars fraction required for the microbial production of ethanol or polyhydroxyalkanoates (PHAs), the polysaccharidic chains need to be separated from the other components and broken down to monomeric sugars. Since phenolic and lipidic compounds can be inhibitory for microorganisms, they should be separated during the pretreatment, allowing for their recovery.

3.1. Chemicals

3.1.1. Tannins

Among winemaking by-products, grape stalks and skins contain a remarkable quantity of tannins (Tables 1 and 2), which can be used as added-value products in food and biomedical or technical applications. For example, tannins from grape stalks are considered good candidates to be used in adhesives [21]. The reason is a high content of procyanidins and prodelphinidins possessing a phloroglucinol-type structure, which is quite reactive in modification reactions with formaldehyde [34]. In this sense, the tannins of grape stems are even preferable to the tannins of wood bark, which also contain less reactive resorcinol-like

structures. In addition, the tannins used in adhesives do not need additional purification, which reduces the cost of the final products. The tannins can also be directly isolated from grape pomaces without separation of the skins, stalks, or seeds [22]. In this case, the tannins' mixture can contain more flavonoids and anthocyanins.

Being difficult to dissolve in organic solvents and in aqueous solutions, the oligomeric/polymeric procyanidins and prodelphinidins can be easily extracted from grape stalks by alkali solutions (NaOH, Na_2CO_3, and $NaHCO_3$) at 70–120 °C [22,64]. This is an inexpensive and effective methodology for the recovery of tannins from grape pomace. However, other isolation processes are also considered prospective for these purposes, for example, supercritical fluid extraction (SFE), microwave-assisted extraction (MAE), and ultrasound-assisted extraction (UAE) [65]. Although the tannin yields were the highest in the extraction trials with 5–15 wt.% NaOH, the best performance in adhesives was demonstrated by tannins extracted with $NaCO_3$ solutions at 100 °C [22,64]. In general, more severe extraction conditions (reactant concentration, temperature, and extraction time) resulted in higher yields but less reactive tannins (with formaldehyde) to produce methylolated structural monomers/oligomers of tannin–formaldehyde resin. Moreover, the acidification of alkaline extracts to isolate the solid residue resulted in less reactive tannins due to the formation of catechinic acid derivatives [22,64]. It was considered that tannin-based adhesives, both the tannin–formaldehyde type and those fortified with diisocyanates, are suitable in biocomposite applications, for instance, in particle boards [22,64]. Methylolated tannins from grape pomaces in combination with glyoxilated organosolv lignin were reported as a prospective adhesive to produce particle boards [66]. Biocomposites produced using tannin-based adhesives showed quite low formaldehyde emissions, which were assigned to the tannins' scavenging effect [64,66]. In fact, when part of the conventional pine fibres (in fibreboards) or particles (in particleboards) are substituted by grape stalk fibres or particles, respectively (Table 4), the formaldehyde emissions decrease four times in fibreboards (from 10.0 to 2.5 mg CH_2O/100 g) and three times in particle boards (from 12.0 to 4.0 mg CH_2O/100 g) (Evtuguin and Cruz Lopes, unpublished results).

Table 4. Properties of biocomposite fibreboards and particleboards produced with grape stalks (Evtuguin and Cruz Lopes, unpublished results).

Properties/Characteristics	Fibreboards [1]	Particleboards [2]
Grape stalk:pine (wt.%)	20:80	40:60
Bulk density (kg/m^3)	753	710
Thickness (mm)	10	10
Urea–formaldehyde resin (wt.%)	8.0	10.0
Paraffin (wt.%)	1.5	-
Bending strength, MOR (MPa)	34.0	55.4
Elongation (%)	8.5	3.3
Internal bond (MPa)	0.54	0.59
Water resistance, ΔW (%)	31.0	25.2
Formaldehyde (mg/100 g)	2.5	4.0

[1] Grape stalk fibres were obtained by vapor pretreatment at 150 °C for 5 min, followed by hot refining. [2] Grape stalks were grinded, and the particle fraction of 1–5 mm was used for the board production.

Tannins extracted from winemaking residues can be introduced in different functional materials. For example, when tannins from red and white grape skins were introduced in packaging barrier films, composed of different modified natural polymers, the films clearly demonstrated bacteriostatic activity against both Gram-negative (*Escherichia coli*) and Gram-positive bacteria (*Listeria innocua*) and were capable of preventing the occurrence of oxidative reactions in sensitive food products [67]. Tannin extract from grape pomaces was combined with silver nanoparticles, resulting in a novel nanomaterial with pronounced antioxidant properties, antimicrobial activity, and antidiabetic potential, which can be used both in technical applications and in biomedical sectors [68].

Tannins in grape skins, especially from red grapes, are considered prospective antioxidants to be used in food applications or in biomedicine [69,70]. The isolation methods for tannins from grape skins (also in the composition of destemmed grape pomaces) are mostly limited to solid–liquid extraction (SLE) with suitable hydroalcoholic solutions, but more advanced techniques, such as SFE and MAE, were recently reported [71]. The obtained extracts can be concentrated and then freeze-dried or dried using spray drying techniques.

Most commonly, grape skins are used for the isolation of tannins from grape pomaces, namely, from red grapes [69–72] and from white grapes [73,74]. Works with separated analyses of the skins and seeds are much less often reported [75]. Practically all the isolated tannin extracts demonstrated strong antioxidant activity and potential health benefits, showing quite high bioavailability and relatively low toxicity [76,77]. Tannins from winemaking residues may be employed to prevent and treat several diseases associated with reactive oxygen species, such as atherosclerosis, coronary heart illnesses, and cancer. The crude extracts from grapes could be used as dietetic supplements for health protection, after defining the dose levels or limits safe for health. However, to be used in medicinal preparations, bioactive components from grape residues should be adequately purified, the structure–activity relations should be established, and the key mechanisms of bioactivities should be well-understood.

3.1.2. Grape Seed and Leaves Oils

Grape seeds from the common grape vine (*Vitis vinifera* L.) are a well-known oilseed crop that contains around 8–20 wt.% (dry basis) of oil. Grape seed oil (GSO) is characterised by a large amount of unsaturated fatty acids (ca. 90 wt.%), particularly linoleic and oleic acids, with traces of linolenic and palmitoleic acids. The remaining are saturated fatty acids, mainly palmitic and stearic acids [78]. Although grape seed residues have been extensively used, the valorisation of vine leaves (a substantial by-product of wine production) has been much less explored. However, these leaves can be a source of interesting bioactive molecules, including phenolic compounds with biological activity, mainly long-chain aliphatic alcohols, triterpenes (e.g., β-amyrin and lupeol), sterols (e.g., β-sitosterol), and tocopherols (e.g., α-tocopherol), which exhibit antioxidant, anti-cancer, and anti-inflammatory properties, among others [79].

Historically, GSO extraction was performed with organic solvents, such as n-hexane. However, this approach is non-selective, as it simultaneously removes pigments and waxes that contaminate the extracts. Additionally, organic solvents are usually toxic for humans and the environment, and this can become an obstacle for food, pharmaceutical, and cosmetic applications, due to strict regulations that require expensive purification and/or waste treatment procedures. Research has focused on mitigating these problems with alternative methods, namely, microwave-assisted extraction (MAE) and ultrasound-assisted extraction (UAE), enzyme-assisted extraction, and supercritical fluid extraction (SFE), which is probably the most successful method [80].

SFE offers significant advantages over conventional extraction with organic solvents. It usually relies on CO_2 as the working solvent due to its mild critical point (73.8 bar and 31.1 °C), widespread availability, null solvent surface tension, inertness, low price, non-toxicity, and safety. Additionally, by manipulating pressure and temperature, its density, viscosity, diffusivity, and solubility parameters can be tuned according to the target material to improve the penetration of the porous matrix, enhance mass transfer, and fine-tune the solvating power. In the particular case of grape biomass, a further synergetic effect can be leveraged as the CO_2 can be obtained from fermentative processes, such as wine production [81].

To improve the yield or selectivity of SFE processes, several pretreatments can be applied prior to extraction. Common treatments include air-drying, freeze-drying, and grinding [82], but more advanced/complex approaches like ultrasound, microwave, enzymatic action (discussed below), and cell explosion by an abrupt pressure drop can be cited [80–83].

Modelling is extremely important for the design, simulation, and scale up of SFE processes. There are several models in the literature to represent the SFE curves, expressed as the cumulative yield, mass of extract against time, or mass of spent solvent. Empirical models may provide reliable fittings but are of limited use, as they provide little insight into the process. Simplified models (e.g., the logistic model, diffusion model, and Brunner model [84]) can provide approximate solutions when information on the kinetics and/or equilibrium is lacking. The comprehensive theoretical approach of phenomenological models provides the most in-depth information on the aspects that influence separation performance, taking into account flow patterns, solute–matrix interactions, accumulation in the bed, axial dispersion, and mass transfer resistances in series and/or in parallel [84–86]. These include the broken plus intact cells (BIC) model, the shrinking core model, and their combined approach [84]. The BIC model [85] is the most adopted approach for the phenomenological modelling of SFE processes.

The SFE of grape parts has been extensively studied by several authors, starting in 1994 with Sovová and coworkers [87] and counting over 70 articles by 2023 (Scopus, using the keywords "grape AND supercritical" for a title search, November 2023). Table 5 gathers selected works covering several types of topics of interest related to the SFE of grape parts. Along with the main features of each piece of research, the supercritical fluid used and the target molecules of interest are also listed. Grape seed is the most studied grape part, followed by grape pomace (the solid remains of grape pressing, also named bagasse or grape marc). The SFE of grape skin [88] and grape vine leaves [79] has also been tested. Research has focused on the effect of the main operating conditions (temperature, pressure, particle size, and cosolvent) [89,90], modelling [91] and optimisation [92,93], comparison with other extraction methods [92–94], scale-up [95], and techno-economic analysis [96].

Table 5. Summarised information on selected scientific articles dealing with SFE of wine industry residues.

Year	Grape Part	Extraction Fluid	Target Compounds	Main Features	Ref.
2000	Seed	CO_2 with ethanol or methanol	Phenolics	Solubility study	[97]
2001	Pomace (skin)	CO_2 with ethanol	Resveratrol	Comparison of grape varieties	[88]
2003	Seed	CO_2 with ethanol	Oil	DoE and scale-up study	[95]
2005	Pomace (skin)	CO_2 with ethanol	Catechin, epicatechim, quercetin, rutin	Effect of pressure and cosolvent	[98]
2007	Pomace	CO_2 with ethanol	Phenolics	Comparison of SFE with SLE	[99]
2007	Seed	CO_2	α-tocopherol	Particle size study	[89]
2009	Seed	CO_2	Oil	Effect of enzymatic pretreatment on SFE	[100]
2010	Pomace	CO_2 with methanol	Phenolic anthocyanins	Supercritical antisolvent extraction	[101]
2010	Pomace	CO_2 with ethanol	Resveratrol	Comparison of SFE with SLE	[92]
2010	Seed	CO_2	Oil (triacylglycerides)	Effect of SFE temperature and pressure	[90]
2010	Seed	CO_2	Oil	Modelling and economic study	[91]
2011	Seed	CO_2	Oil	Modelling of extraction curves	[102]
2012	Seed	CO_2	Oil	Scale-up study and economic evaluation	[96]
2013	Pomace	CO_2 with ethanol	Polyphenol	Effect of pressure and economic study	[103]

Table 5. *Cont.*

Year	Grape Part	Extraction Fluid	Target Compounds	Main Features	Ref.
2014	Pomace	CO_2 with ethanol and/or water	Phenolics (proanthocyanidins)	Sequential extractions with CO_2/water and CO_2/ethanol	[104]
2015	Pomace	CO_2	Polyphenols	UAE combined with SFE	[105]
2015	Seed	CO_2	Oil	Optimization using DoE	[93]
2016	Seed	CO_2	Oil	Comparison of grape cultivars oil content	[106]
2017	Pomace	CO_2	Phenolics	Techno-economic comparison of subcritical water extraction, SFE with CO_2, and SLE	[94]
2019	Pomace	CO_2	Oil	Scale-up study and economic evaluation	[107]
2020	Vine leaves	CO_2 with ethanol or ethyl acetate	LCAA, triterpenes, sitosterol, tocopherol	Effect of cosolvent, temperature and biomass particle size	[79]
2023	Pomace	CO_2 with water	Phenolics, polysaccharides	Water as cosolvent	[108]
2023	Pomace	CO_2	Glycosylated and lipidic compounds	Combined pulsed electric field and SFE process	[109]
2023	Pomace	CO_2	Phenolics, sterols, fatty acids	Combined pulsed electric field and SFE process, comparison with cold pressing	[110]

LCAA: long-chain aliphatic alcohols; DoE: Design of Experiments; SLE: solid–liquid extraction; SFE: supercritical fluid extraction; UAE: ultrasound-assisted extraction.

SFE of Grape Seed Oil

Passos et al. performed the extraction of GSO at 180, 200, and 220 bar, 313.15 and 323.15 K, and a CO_2 flow rate of 1.7×10^{-4} kg s^{-1} [90]. After 6 kg of CO_2 (about 10 h), all experiments achieved a maximum oil extraction yield of 11.5%. As seen in Figure 5, the extraction rate increased with increasing pressure and decreasing temperature, with the run conducted at 220 bar and 313.15 K attaining the maximum extraction yield in only 4 h (2.5 kg of CO_2 consumed). It was concluded, upon estimation of the solubility and the convective mass transfer coefficient, that these results could be mainly attributed to the solubility and that the convective mass transfer coefficient played a minor role in the process [90].

The triacylglycerides content was measured and appeared to be mostly unaffected in the range of the assessed operating conditions. In contrast, the antioxidant capacity of GSO (evaluated in terms of tocopherol equivalents) varied with pressure and significantly varied with temperature. The antioxidant activity is more pronounced on the oil collected during the first stages of the process, where 35–40% of the total oil is extracted.

Passos et al. tested the possibility of enhancing the SFE of GSO by applying an enzymatic treatment to milled seeds, prior to extraction, aiming to increase oil availability [100]. This pretreatment was isothermally performed at 40 °C, under continuous stirring for 24 h, with a cell-wall-degrading enzyme cocktail containing cellulase, protease, xylanase, and pectinase [111]. The SFE was then conducted at three different pressures (160, 180, and 200 bar) with a fixed temperature (313.15 K) and CO_2 flow rate (1.7×10^{-4} kg s^{-1}). Figure 6 compares the extraction curves for untreated and pretreated grape seeds. Pretreated seeds' extraction resulted in a maximum total yield of 16.5%, which is 44% higher than the best result obtained for untreated seeds under the same operating conditions [100]. This result supports the hypothesis of the broken plus intact cells (BIC) model proposed by Sovová for seed oil extraction, which considers the ratio of broken and intact cells in the extractor [85,87]. Similar to what occurred with untreated seeds, pressure remains

a major factor for the extraction rate, with higher pressures requiring lower amounts of CO_2 (or less time) to attain the maximum yield. As pressure rises, the initial part of the cumulative extraction curves of the treated and untreated biomass become closer, tending to overlap. This indicates that an enzymatic treatment may be especially beneficial in an industrial setting, where short extraction times and lower operating pressures are usually economically optimal.

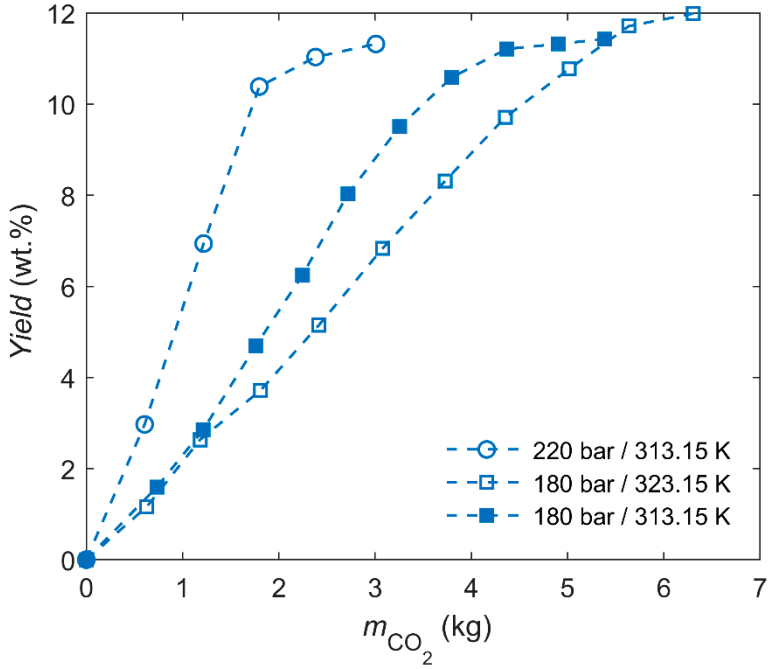

Figure 5. Extraction curves for SFE of grape seed oil with CO_2. Adapted from [90].

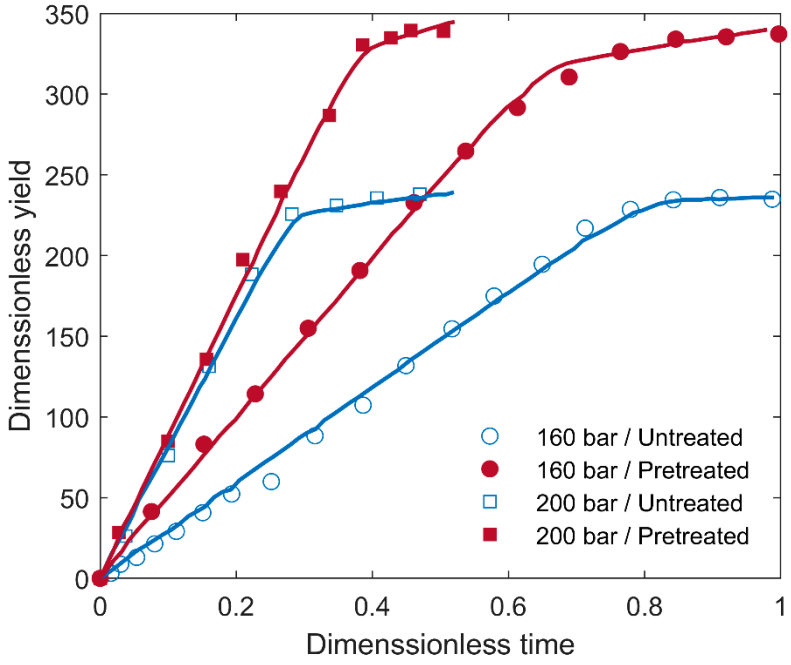

Figure 6. Extraction curves for untreated and enzymatically pretreated grape seeds, at 313.15 K and 160 bar and 200 bar. The symbols denote experimental results, and the lines represent the BIC modelling results. Adapted from [102].

Passos et al. were able to successfully model the experimental extraction curves of untreated and enzymatically pretreated grape seeds using the BIC approach. The modelled curves are presented in Figure 6 (lines) and show average absolute relative deviations between 2.30% and 7.25% [102].

SFE of Grape Vine Leaves

The SFE of grape vine leaves was performed in a 0.5 L lab scale extractor at three different temperatures (40, 60, and 80 °C) and a constant pressure (300 bar) and CO_2 flow rate (12 g min^{-1}). Ground (d_p < 1 mm) and crushed (d_p < 10 mm) leaves were tested as well as two cosolvents, ethanol and ethyl acetate, with concentrations of 5 and 10 wt.% [102]. For these operating conditions, the total yield ranged from 1.86 to 7.52 wt.%. The best results were obtained for ground particles, with 10 wt.% ethyl acetate cosolvent and 80 °C.

Regarding the target compounds, SFE provided individual yields up to 0.42 wt.% for the group of long-chain aliphatic alcohols, 0.19 wt.% for triterpenes, 0.06 wt.% for β-sitosterol, and 0.04 wt.% for α-tocopherol. The use of ethyl acetate (10 wt.%) as the CO_2 cosolvent showed very interesting results for the extraction of triterpenes, with yields higher than Soxhlet extractions with dichloromethane, ethanol, or ethyl acetate. At the same time, very high selectivities were attained for triterpenes (lupeol and β-amyrin), starting at 1.7 in the initial hour of extraction and increasing over time to values between 10 and 100. It was concluded that the particle size and cosolvent addition played a significant role in the selective removal of target compounds from the biomass.

3.2. Biofuels

In opposition to fossil fuels, biofuels from biomass or renewable resources allow a solid geographical autonomy for the energy supply, instead of the dependent position of most states [112]. However, the replacement of fossil fuels by renewable ones in the transport sector needs the development of efficient and sustainable industrial processes for their production. Furthermore, due to growing awareness of environmental pollution effects on climate change and humanity's health, there is increasing pressure for decarbonisation that leads to several new regulations, aiming to shift the utilisation of fossil fuels to biofuels and envisaging a more sustainable world [113].

The traditional production of bioethanol from renewable feedstocks, namely, corn in the USA and sugarcane in Brazil, is associated with lower greenhouse gases emissions but generates a food–fuel competition. Besides this denominated first-generation bioethanol (i.e., based on food crops), alternative second-generation bioethanol is produced from biomass residues or industrial waste streams, thus meeting environmental goals and increasing sustainability [114]. Natural residues are available in large amounts and are usually composed of lignocellulosic biomass [115] continuously generated in agricultural lands, forests, and fields. Wastes such as municipal waters and the by-products continuously released in industrial plants are also renewable resources that can be used as feedstock in new bioprocesses for biofuel production. Residues of wine vinery wastes were recently investigated, through conversion to biofuels and other valuable products, aiming for their valorisation and simultaneously decreasing the environmental impact of winemaking [3].

Among several biofuels, hydrogen has been highlighted due to its high energy content and its clean combustion, with research focusing on its production, utilisation, and storage/transportation. Bioprocesses based on the fermentation of vinery residues have been already studied, reporting pomace as a rich source of sugars' substrate and, simultaneously, a source of endogenous microbial inoculum. Research work on biohydrogen production has been performed, establishing different strategies. For instance, the dark fermentation of grape must deposits was performed under the same conditions using either its endogenous inoculum or an external microbial inoculum [116]. The results revealed that grape must residues could be applied, without any heat treatment, either as the substrate or as the microbial consortium for endogenous fermentation for hydrogen production and that the efficiency was similar to that obtained by adding an external heat-treated inoculum [116].

Photofermentation (i.e., the fermentation of carbonated organic compounds performed by photosynthetic bacteria or microalgae under light and anaerobic conditions) was also researched, showing the big interest in agricultural-waste-based bioprocess opportunities and challenges [117].

Biomethane is a gaseous biofuel, as well as being the cheapest one, that can be produced through the traditional anaerobic digestion of organic carbon residues. The direct utilisation of produced biogas has been widely implemented in poultry, livestock, and agricultural activities for many years [117]. Recently, sustainability issues related to food waste management increased the research on the produced biogas (or that can be produced) in several industries, including wineries [118]. Biomethane's production based on grape pomace, pulp, and seeds was studied, and the results showed a positive effect when a mechanical pretreatment (e.g., grinding) was performed before the main anaerobic process and that pomace was the best substrate for higher methane production [119]. After preliminary batch tests, a scaled continuous pilot test was performed with improved results, namely, a higher yield of methane (ca. 81% higher) even without the pretreatment [119]. Recently, to reduce the dependence on fossil fuels coming from Russia, the European Union has been promoting biogas production around all European countries to boost an upgrade to biomethane. New targets are coming out concerning increased biomethane production and accelerating hydrogen research and development for future implementation [120]. In 2022, the European Commission approved the REPowerEU plan that set a goal of an annual increase in the production and use of sustainable biomethane to 35 billion cubic meters by 2030, using forest and agricultural residues as feedstocks, thus protecting land use and food production. An industrial partnership is working and researching to attain this EU objective [121].

Second-generation bioethanol production was the focus of many researchers in the face of the rise in fossil fuels' prices and the decrease in reserves, besides the known geopolitical limitations. Different lignocellulosic raw materials, including industrial waste streams rich in pentose and/or hexose sugars and sequential or co-cultures of fermenting yeasts, have been assayed [122,123], and promising results are published day by day. There are several publications on bioethanol from food and agricultural waste feedstocks, but studies for bioethanol from winery residues are scarce. Rodríguez and co-workers studied grape pomace and beet pomace solid-state fermentation by *Saccharomyces cerevisiae* PM-16 and made a comparison with beet juice liquid fermentation [124]. The best results for monosaccharides' release and bioethanol yield were reported for grape pomace, and the authors encourage studies for the scale-up of solid-state fermentation [124]. Envisaging bioethanol production, Corbin and co-workers assayed pomace for soluble sugars' recovery and for acidic or thermal hydrolysis. After detailed composition analysis of pomace, its pretreatment, and its saccharification, the authors concluded that pomace valorisation for bioethanol production has high potential, predicting the production of 400 L of ethanol per tonne of pomace [125].

The integral valorisation of grape skins to produce three types of products such as bioethanol by *S. cerevisiae* 4072 fermentation, oleanolic acid, and low-density boards for insulation was reported [30]. Initially, grape skins were extracted with a water–hexane mixture (1:1 *v*/*v*; solid-to-liquid ratio of 1:10), the organic phase containing the oleanolic acid was removed, and the aqueous phase rich in sugars was forwarded to acid hydrolysis. The solids were separated and used to produce the insulating board, while the obtained aqueous monosaccharides were submitted to yeast fermentation. The theoretical ethanol yield of 0.51 g ethanol/g sugars was attained, and the authors estimated a production of 310 L ethanol per tonne of grape skins [30].

Recently, Atatoprak and co-authors studied the valorisation of grape stalks, performing alkaline pretreatment and hydrolysis with diluted acid and enzymes [25]. Bioethanol production by both *Pichia stipitis* DSMZ 3651 and *S. cerevisiae* DSMZ 70449 attained low bioethanol yields (e.g., 0.24 g ethanol/g sugars), certainly due to the inhibition effect of grape stalks' recalcitrance on both yeasts [25]. In another study, after the first step of grape

stalks' washing, an autohydrolysis pretreatment was introduced to release fermentable sugars: different hydrolysates and synthetic media fermentations were compared, and the authors concluded that the fermentation of hydrolysates always provided better results when compared to synthetic media, due to the presence of other nutrients in the hydrolysates. Among other fermentation products, bioethanol was the most concentrated [126].

The simultaneous saccharification and fermentation of vine shoot waste by *S. cerevisiae* YSC2 was investigated after performing an autohydrolysis pretreatment and/or chlorite delignification of the solid fraction. Autohydrolysis at 165 °C, followed by chlorite delignification and by the integrated saccharification and fermentation process (at 37 °C, with 10 wt.% solids loading, for 72 h) provided 60 g/L of bioethanol [127]. The sequential saccharification and fermentation of vine shoots' waste, pretreated by two sequential autohydrolysis steps (with increased severities), yielded 96% ethanol (83% for the simultaneous saccharification and fermentation) and provided four different final products, namely, xilooligosaccharides, phenolic compounds, lignin, and bioethanol (13.7 g, 3.1 g, 27 g, and 13.1 g per 100 g of vine residues) [128].

The grape stalks' fibrous residues were considered a promising biofuel able to compete with softwood [129,130]. The carbon content and the high heating value of softwood and grape stalks are quite similar (about 50 wt.%; 19.6 and 19.1 MJ/kg, respectively), but the stalks contain almost 10 times more ash (0.3–0.5 wt.% in wood vs. 3–6 wt.% in grape stalks) and a higher moisture content (8–9 wt.% in wood and 13–14 wt.% in grape stalks). The specific consumption of energy for pelletising grape stalks' particles was found to be approximately 25% lower when compared to softwood sawdust [129]. Table 6 summarises the most important properties of the pellets produced with grape stalks' particles and softwood sawdust. The bulk density, particle density, and durability are quite similar. The high heating value of grape stalks' pellets was just slightly lower (16.7 MJ/kg) than that obtained for softwood pellets (18.2 MJ/Kg), the difference being explained by the higher humidity and ash content of grape stalks' pellets [129]. Other researchers reported similar results for the main properties of stalk pellets obtained from different red and white grape varieties. However, the differences among them, in terms of the specific energy consumption for pelletising, were not specified [130]. The general analysis of life cycle assessment revealed that heat from grape stalks' pellets is more environmentally friendly than heat from wood pellets, for 7 out of 11 impact categories, including marine aquatic ecotoxicity, which is considered the most critical impact category [131].

Table 6. Physical characteristics of grape stalk pellets and softwood pellets [130].

Parameter	Softwood Pellets	Grape Stalk Pellets
Water content, wt.%	8.10	12.6
High heating value, MJ/kg	18.2	16.7
Low heating value, MJ/kg	16.6	15.3
Length, mm	16.7 ± 2.5	17.4 ± 1.2
Diameter, mm	6.06 ± 0.04	5.89 ± 0.07
Bulk density, kg/m^3	660 ± 10	670 ± 2
Particle density, kg/m^3	1098 ± 47	1129 ± 47
Energy density, MWh/m^3	3.05	2.85
Durability, %	95.6	95.8
Specific energy consumption for pelletising, kWh/kg	0.137	0.110

3.3. Polymers

Wine wastes have been used as the substrate for microorganisms or to produce composite materials. The literature has several examples of materials that were obtained by microbial production from wastes by direct synthesis or by the synthesis of the monomers that are later chemically polymerised. The former corresponds to PHAs and bacterial cellulose (BC) and the latter to polylactic, γ-polyglutamic, or poly(butylenesuccinic) acids [8,132].

Our group has experience in PHAs and BC production from wine wastes, and these are the bacterial polymers chosen to be reviewed in this section.

3.3.1. Polydroxyalkanoates

Polyhydroxyalkanoates (PHAs) are polyesters of various hydroxyacids. PHAs were reported to be produced by more than 300 genera of prokaryotes in nature [133]. So far, 100 different monomers of PHAs were already identified, the majority being 3-alkanoic acids (3HAs) and linear and saturated molecules covering a range from 3 to 16 carbon atoms [134]. PHAs are usually classified based on the number of carbons of their monomers, being designated short-chain length (scl-PHAs) and medium-chain length (mcl-PHAs) when the number of carbons is 3–5 and 6–14, respectively. PHAs are intracellularly accumulated as complex inclusion bodies or granules by microorganisms when facing unbalanced conditions in their living environment, such as the limitation of oxygen or nitrogen or a marked variation in carbon availability. Under these conditions, microorganisms produce PHAs to act as a carbon source when external conditions favour growth [135]. This ability is an important competitive advantage that allows PHAs producing organisms to thrive [136].

Biodegradability and biocompatibility are properties that make PHAs environmentally friendly materials with a wide range of applications, from packaging to medical devices [136]. The number of carbons of the monomers defines some of the PHAs' characteristics; for example, scl-PHAs are thermoplastics with higher melting points and crystallinities than mcl-PHAs, which are elastomers [137]. PHAs' composition, properties, or chains' size can be tailored by selecting the proper carbon sources, organisms, and reactor operational conditions [138].

PHAs share similar characteristics with common plastics, which led to their industrial production. However, PHAs' production is still very low when compared to other alternatives to common plastics, since the production costs are still high [139]. The attempts to lower these costs include the use of cheap and suitable substrates, since the few existing industrial processes still rely on expensive and defined media with pure carbon sources that correspond to 38–50% of the final costs of PHAs [9]. The use of inexpensive and non-food competitive raw materials, such as industrial wastes, is a real possibility for decreasing PHAs' production costs. A diversity of wastes, like whey from the cheese industry, sugar molasses, liquors from pulp and paper, olive mill wastewaters, or wastes from fruit processing, was already tested [139]. As for wine wastes, despite being cheap and abundant, only a few articles report their use as a carbon source for the biosynthesis of PHAs, and most of these works used grape pomace (Table 7).

So far, the main types of PHAs obtained from grape pomace have been poly-3-hydroxybutyrate (P(3HB)) and mcl-PHAs (Table 7). P(3HB), a homopolymer of the acid 3-hydroxybutyrate, which is the most common PHA in nature. P(3HB) was obtained using the bacteria *Cupriavidus necator*, considered one of the most efficient PHAs' producers, which is, consequently, the most studied. Most bacteria only convert monosaccharides to P(3HB), but *C. necator* is more versatile and can use other components, such as short-chain organic acids like acetic, propionic, butyric, valeric, and caproic acids [140].

PHAs' production was designed as a step toward a grape-pomace-based biorefinery where other products could be produced [140,141]. Besides short-chain organic acids and P(3HB), other obtained products include polyphenols, methane [140], lipids, pigments, phenolic compounds, lignin, and cellulose [141]. It is worth noting that, despite the differences in the substrate being used (red or white grape pomace) and in the pretreatment method, the amount of P(3HB) produced by *C. necator* was similar, 68% and 63% of the cell dry weight (cdw), respectively [140,141]. In our research group (unpublished results), the hot water extraction of grape pomace was used to obtain a sugar-enriched fraction that was fed to two different strains of *C. necator* (DSM 545 and DSM 531), which efficiently converted the extracted monosaccharides, producing a PHAs content of ca. 85% cdw. The product's diversity not only contributes to increase the biorefinery's profit but also can

contribute to its energetic efficiency with the methanisation of the remaining organic matter of the process [140].

From the processing point of view, P(3HB) is not very attractive due to its low flexibility. For this reason, many researchers have focused on the production of mcl-PHAs with a wider range of applications [142]. Bacteria from the genus *Pseudomonas* are the few examples of natural producers of mcl-PHAs, and two strains, *P. resinovorans* and *P. putida*, were tested with monosaccharides extracted from grape pomace [142,143]. A PHAs content of 23.3% cdw was obtained after the enzymatic conversion of the residual polysaccharides of white grape pomaces and the conversion of the obtained monosaccharides in a batch reactor with *P. resinovorans* [142]. The same authors tried to upscale the process in a fed-batch system, using *P. putida* KT2400 and sugars extracted from grape pomace with water, which resulted in a PHAs content of 77% [142].

More recently, extremophiles, namely, thermophiles and halophiles, have attracted much attention, since the necessity of sterility can be lowered due to the higher temperatures and high salinity, respectively, required by these bacteria. Under these conditions, common microbial contaminants cannot survive, and only extremophiles can thrive. The halophiles *H. halophila* and *H. organivorans* were successfully tested for PHAs' production with sugars obtained from enzymatic hydrolysis after phenolics' extraction of white grape pomace with a medium containing a NaCl concentration of 6.6% and 8.0%, respectively. The P(3HB) was always obtained, and the cell contents obtained were 57.0% of cdw and 55.4% of cdw, respectively, which were better than that obtained with *C. necator*: 47.2% of cdw, also in shake flasks [141]. The thermophile *T. taiwanensis* was tested for PHAs' production under 50 °C with sugars released from the enzymatic hydrolysis of pomaces of different varieties of red, white, and rose grapes as the substrate. The best result was obtained with white grape pomace with P(3HB) production, reaching 47.9% of cdw [144].

Since grape pomace is solid, recently a solid-state fermentation (SSF) has been attempted, instead of the traditional suspended cultures, in a separate hydrolysis and fermentation process [145]. The process started with the hydrolysis of white grape pomace promoted by *A. niger* to facilitate the access of the PHAs-producing bacteria to the carbohydrates. Then, *C. necator* was used also in SSF and produced P(3HB), corresponding to a content of 21.3% of cdw [145].

Wine lees were also used in PHAs' production. Firstly, they were tested as a substitute for commercial yeast extract to decrease the cost of medium preparation [62]. Since wine lees are the solid residue formed after the fermentation step, besides components from grapes they also contain the remainder of the fermentative yeasts, which significantly contributes to the nitrogen content of the waste. After hydrolysis using the non-purified enzymatic extract of *Aspergillus oryzae*, the hydrolysate was mixed with crude glycerol, the main carbon source, and fed to *C. necator*. The bacteria were able to grow and produce P(3HB), showing that hydrolysed wine lees could be a cheaper alternative to the use of commercial supplements [62]. More recently, wine lees have been used as a carbon source for an anaerobic digestion process, to convert them to carboxylic acids. Then, the mixture of carboxylic acids was fed to an enriched photoheterotrophic mixed culture. A copolymer of 3-hydroxybutyrate and 2% of 3-hydroxyvalerate was obtained, corresponding to a PHAs content of 40.0% [146].

Table 7. Overview of PHAs' production processes using grape pomace as substrate.

Type of Grapes	Pretreatment	Bacteria	Carbon Source *	Process Configuration	PHA (g/L)	PHA (%cdw)	Prod (g/L.h)	Type of PHA	Ref.
White	Enzymatic hydrolysis	*Pseudomonas resinovorans* (DSM 21078)	M	Batch in bioreactor	21.3	23.3	0.05	mcl-PHA	[142]
White	Water extraction	*P. putida* KT2400 (ATCC 47054)	M	Fed-batch pilot scale bioreactor	21.8	77	0.10	mcl-PHA	[143]
Red	Extraction with $scCO_2$ + anaerobic digestion	*Cupriavidus necator* (DSM 545)	O	Fed-batch	n.d.	68	n.d.	P(3HB)	[140]
White	Enzymatic hydrolysis after phenolics extraction	*C. necator* H16 (CCM 3726)	M	Batch in bioreactor	8.3	63.0	0.28	P(3HB)	[141]
		Halomonas halophila (CCM 3662)		Batch in shake flasks with NaCl 6.6% (*w*/*w*)	1.8	57.0	0.025		
		Halomonas organivorans (CCM 7142)		Batch in shake flasks with NaCl 8.0% (*w*/*w*)	2.1	55.4	0.029		
White	Enzymatic hydrolysis after phenolics extraction	*Tepidimonas taiwanensis* (LMG 22826)	M	Batch in shake flasks at 50 °C	2.09	47.9	n.d.	P(3HB)	[144]
Red					0.022	8.4	n.d.		
Rose					0.236	12.3	n.d.		
Not reported	Solid state enzymatic hydrolysis	*C. necator* (DSMZ 428)	M	Solid-state fermentation in shake flasks	n.d.	21.3	n.d.	P(3HB)	[145]
Red	Acidogenic fermentation	*P. putida* (DSMZ 6125)	O	Fed-batch pH-stat mode	10.4	61	0.21	mcl-PHA	[10]
White	Hot water extraction at 100 °C, 2 bar	*C. necator* (DSM 545)	M	Batch in shake flasks	5.48	86	-	P(3HB)	This study
White	Hot water extraction at 100 °C, Patm	*C. necator* (DSM 531)	M	Batch in bioreactor	2.19	85	0.03	P(3HB)	This study

* carbon sources; M = monosaccharides; O = organic acids; cdw = cell dry weight; prod = volumetric productivity; patm = atmospheric pressure.

3.3.2. Bacterial Cellulose

Most of the cellulose on Earth is of vegetable origin, but this is not the only source. Few genera of bacteria can produce it, and, for this reason, it is called bacterial cellulose (BC). Microorganisms usually secrete BC to the air–liquid interface with a nanofibrillated structure, forming films that cover the liquid surface [147]. BC is a polysaccharide produced completely free of lignin and hemicellulose, facilitating its extraction and purification. It also presents a high degree of polymerisation, good biocompatibility, biodegradability, high crystallinity, and excellent mechanical properties [148]. Its fibres have a very high surface area per mass unit and are of a hydrophilic nature. BC is extensively used in many fields, including biomedical materials, drug delivery, tissue engineering, the food industry, acoustic diaphragms, functional paper, optical displays, nanostructured biomaterials, and biocomposites [148].

The nutritional medium usually accounts for 30% of the total production costs, and it is one of the main challenges for the implementation of BC industrial production [149]. For this reason, cheap feedstocks, such as industrial wastes, were tested as carbon and other nutrient sources to produce BC (Table 8). Wine wastes, namely, grape pomace, were among the tested residues. Contrary to what was found for PHAs, the main carbon source used for BC production extracted from grape pomace was monosaccharides. Usually, the monosaccharides were extracted with water, at different temperatures, and only one author reported their extraction with citric acid at pH 5.0 [147], as summarised in Table 8.

Table 8. Overview of BC production processes using grape pomace as substrate.

Type of Grapes	Pretreatment	Bacteria	Process Configuration	BC (g/L)	Ref.
White	Water extraction, at 100 °C	*G. sacchari*	Static incubation in Erlenmeyer	0.63	[150]
White	Water extraction, at room temperature	*K. xylinus* DSM 6513	Static incubation in Erlenmeyer	8.0	[151]
White	Acidic extraction, at pH = 5 and at room temperature	*K. xylinus* DSM 6513	Static incubation in Erlenmeyer	6.56	[147]
White	Water extraction, at 70 °C	*K. xylinus* DSM 6513	Static incubation in plates	0.67	[152]
Red	Water extraction, at 70 °C	*K. xylinus* DSM 6513	Static incubation in plates	0.28	[152]
Red and white	Water extraction, at 40 °C	*K. sucrofermentans* DSM 15973	Static tray reactors	9.0	[153]

Carreira and co-workers separated grape skins from grape pomace and, after extraction with water at reflux temperature, obtained an extract enriched in glucose and galactose that was used to produce BC using the bacterium *Gluconacetobacter xylinus* isolated from kombucha tea [150]. In all the reviewed works, BC was produced under static conditions that allowed for obtaining films of this polysaccharide. The structure of BC is known to be deeply influenced by the operational conditions, and the application of stirring results in BC in the form of pellets. However, the film structure is much more interesting from the processing point of view [147].

Other authors attempted to extract monosaccharides at temperatures lower than 100 °C, which would be much more interesting from the economic point of view (lower energy required), but the BC concentrations were lower. For instance, the sugar concentration obtained after water extraction at 100 °C was 46.0 g/L [150], whereas at room temperature it was 37.6 g/L [151] and at 40 °C it was 26.9 g/L [153]. The extraction with citric acid yielded a concentration of 60 g/L [147].

Grape pomace from white wine production was the preferred feedstock in the reviewed works. Only one of the authors used mixed waste from different varieties of grapes [153], and another [152] used red grape pomace to compare the production of BC using red and white grapes. As expected, the red grapes led to lower values of produced BC, due to the lower availability of monosaccharides, but the authors did not reveal the sugar concentrations obtained after extraction [152].

A strategy to completely utilise grape pomace and not only the extracted monosaccharides was developed in 2021 [153]. These authors proposed an integrated biorefinery using different streams of wine wastes, namely, grape pomace, grape stalks, and wine lees. Besides BC produced from the sugars extracted from grape pomace, *Komagataibacter sucrofermentans*, GSO, ethanol, crude tannins, and tartaric acid were some of the obtained products. Succinic acid was produced by *Actinobacillus succinogenes* from the sugars' fraction obtained after the delignification and enzymatic hydrolysis of grape stalks [153].

BC and PHAs are good examples of materials that can be produced from wine wastes. However, there is still much work to be accomplished for integrating the processes into a biorefinery or for scaling up the processes. The works published so far used pure bacterial cultures that have a high impact on the cost of the process, because it is necessary to use sterile conditions and tight control. In the case of PHAs, it is possible to use mixed microbial cultures with undefined compositions that thrive in environments where the ability to produce PHAs signifies a competitive advantage. A wide variety of wastes were already tested with this type of culture [142], but, to our knowledge, wine wastes have not been assessed yet. Regarding BC, some microbial consortia are known to be able to produce it, since most of the species with that capacity were isolated from the bacterial community that developed in kombucha tea [154]. Nevertheless, the amount of BC produced from wastes still needs to be improved, since low productivities and yields have been obtained so far [155].

4. Future Perspectives

The development of waste-based bioprocesses has several challenges that are easily recognised when dealing with wine wastes. From the heterogeneity and complexity of the feedstock to its seasonality, including the necessity of transportation or the small amounts produced (most wineries are SMEs), these challenges need to be addressed before establishing the processes. Ideally, the establishment of biorefineries, ensuring the complete utilisation of wastes, should be the main goal to face environmental issues and to improve decarbonisation. In this way, the obtained products (chemicals, materials, and fuels) would enlarge the profit of the wine companies, reduce the environmental impact, and contribute to the energetic capability of the industrial plant.

Despite the low diversity of wastes, each of them can present significant differences depending on the grape variety, on land characteristics, and on the weather conditions during the development of the grapes. This is especially critical at the levels of sugars, phenolics, and acidity [156,157]. This heterogeneity and complexity of the feedstock should be considered when selecting the type of bioprocess and the required pretreatment steps. The inclusion of pretreatment steps should be carefully planned, since it signifies additional costs for the process: mainly equipment and chemicals. As reviewed in this article, the fractionation of the wastes can act as a pretreatment step. As an example, the polysaccharides of grape pomace can be microbially converted to short-chain organic acids and then to PHAs [142]. However, the polyphenols of grape pomace can act as inhibitors in bioprocesses. By applying supercritical CO_2 extraction to grape pomace, the separation of polyphenols was achieved, avoiding the inhibition of subsequent bioprocesses, and, at the same time, commercially valued compounds were obtained [2]. The developed process should guarantee the quality of the final product, despite variations in the characteristics of the feedstock.

The complexity of each wine waste and the several steps necessary for its complete processing, according to the circular economy concept, only make sense in a biorefinery.

However, the establishment of a biorefinery for each wine-making industry might not be economically feasible, since most Portuguese wine companies are SMEs [13] with low amounts of wine being produced and, consequently, waste being generated. Most of the wastes in Portugal are directed to nutrient recycling and composting, but the preferred method is chosen based on the costs of the technology. Unfortunately, some small companies, due to the associated high costs, prefer to make illegal waste disposal either in landfills or sewage, despite the high fines associated, as reported in 2016 [2].

Since 2008, in the European Union, before disposal, wineries are obliged to send grape pomace and wine lees to distilleries for ethanol and tartaric acid recovery (EC no. 479/2008). The recovery of the two compounds is the first step for the valorisation of the two wastes, representing a significant economic benefit, even with the associated transport costs [2].

The limitation of waste management to nutrient recycling and controlled disposal is general in the wine industry. The majority of the life cycle analyses (LCAs) of the wine industry barely mentions the generated waste, ignoring the possibility of obtaining added-value products [158]. This probably results from the fact that the carbon footprint attributed to solid waste only corresponds to 1.7%, when compared to the 45.6% for bottle making or the values obtained for the respective electricity production, considering the full cycle of production of one bottle of wine [159]. As shown by the present revision, this paradigm will change in the future due to the potential of winery wastes as a source of valuable products. One of the most recent LCAs of the wine industry already considered the possibility of valorising the generated wastes, including two side processes for the extraction of grape seed oil besides tartaric acid [160].

There are already several proposals for the establishment of a biorefinery for wine wastes [3,4,10,140,153]. Most of them agree on the main problems to overcome and the necessity of diversifying the obtained products. A biorefinery using grape pomace, grape stalks, and wine lees was proposed by Filippi et al. [153]. The process included an initial extraction of valuable compounds like ethanol, phenolics, tannins, grape seed oil, antioxidants, and tartaric acid, followed by the biological production of bacterial cellulose and succinic acid from the carbohydrate fractions [153]. A red-grape-pomace-based biorefinery that would allow for obtaining polyphenols, fatty acids, PHAs, and biogas was proposed by Martinez et al. [140]. A biorefinery with grape seeds as feedstock to obtain bioactive compounds by extraction and energy from the remaining biomass was also proposed [161].

As reviewed, the different technologies for the use of wine wastes are still in the early stages of development so, more research is required to establish them at the commercial scale. This research should focus on the development of biorefineries and on processes' scaleup. Since most of the processes are still at the laboratory level of development, the transition to the industrial scale is mandatory as soon as possible [3]. However, this is not enough to guarantee the commercial success of the process. Government policies and investment incentives would help the application of technologies based on wine residues [162].

Another bottleneck associated with the valorisation of wine wastes is the seasonality of wine processing. In Europe, it occurs during a specific period of the year (from August to November), which signifies that there is no waste generated during the rest of the year. To overcome this situation, a strategy that would allow for collecting wastes from several companies in specific places should include efficient transportation and storage systems. Implementing both systems has a significant economic impact, and this would be a determinant for the biorefinery operation. The problems and associated costs either with transportation or with the storage of waste could result in their degradation, not allowing the production of the desirable valued compounds [163].

Considering all these pros and cons, a new type of biorefinery that would allow for the sequential processing of wastes from various seasonable products is proposed. This biorefinery, besides winemaking wastes, should use, as feedstock, other classes of wastes resulting from agroactivities' processes like olive oil production, diverse seasonal fruit processing, and forest or food crops' cleaning activities, among others. The most

appropriated wastes to be supplied to this versatile biorefinery should be researched, planned, and developed according to their seasonal availability, the products' demand or value, and the regional incentives for waste management policies. These last two should be the drivers for the implementation of efficient biorefineries contributing to the low-carbon economy and climate change mitigation, according to the circular economy model.

5. Conclusions

The main wastes from the wine industry were reviewed in terms of their abundance, chemical composition, and eventual use for the production of added-value products. Despite their complexity and, in some cases, the incipient stage of research of their valorisation (e.g., wine lees), these wastes are promising raw materials that allow for obtaining products with a wide range of applications. The numerous processing approaches outlined in the biorefinery concept should enable the wine industries to gain additional profits. In this case, not only would the concept of the circular economy be fulfilled but also some advantages could be anticipated, namely, the increase in revenues, the reduction in waste disposal costs, and the expansion of the product portfolio. Regarding the impact of the wine industry on the Portuguese economy, the establishment of wine-waste-based biorefinery chains would also create additional profits for the country. However, several aspects related to the cost-effectiveness of the proposed solutions need to be addressed, such as the small size of most Portuguese wine companies and the seasonality of winemaking activities. It is noteworthy that most of the reviewed processes are still in development on a laboratory scale, requiring adequate scaling-up efforts, economic analysis, and life cycle assessment. However, the approaches demonstrated for the utilisation of winemaking residues illustrate to the industrial and scientific community the pathways of winemaking wastes' processing and valorisation. The combination of these residues with other classes of residues could be a possible strategy for the implementation of new efficient biorefineries that contribute to the low-carbon economy.

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