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Review

Fermentation-Based Valorization of Grapevine Waste: Microbial Bioconversion, Bioactive Recovery, and Industrial Bioprocess Integration

Emanuel Vamanu [1,2,*], Laura-Dorina Dinu [1] and Alina Orțan [3]

[1] Faculty of Biotechnologies, University of Agronomic Sciences and Veterinary Medicine of Bucharest (USAMV Bucharest), 011464 Bucharest, Romania
[2] Anoom Laboratories SRL (Greenbiom®), 077190 Voluntari, Romania
[3] Faculty of Land Reclamation and Environmental Engineering, University of Agronomic Sciences and Veterinary Medicine of Bucharest (USAMV Bucharest), 011464 Bucharest, Romania
* Correspondence: emanuel.vamanu@bth.usamv.ro; Tel.: +40742218240

Abstract

Vineyard management and winemaking leave behind large residue streams that are still rarely used as fermentation feedstocks. This review considers how pomace, skins, seeds, stems, canes, pruning wood, leaves and wine lees can be directed toward microbial bioconversion, fermentation-assisted recovery of bioactive compounds, and circular biorefinery schemes. Their composition (phenolics, stilbenes, dietary fiber, lignocellulose, sugars, minerals and yeast-derived material) makes them workable in either solid-state or submerged fermentation. We describe the routes that lead to enzymes, organic acids, ethanol, microbial biomass, biosurfactants, pigments and functional ingredients, together with the mechanisms by which bound phenolics are released and transformed. Green extraction, downstream purification, analytical standardization and process intensification are treated next, since market-ready consistency depends on them. The remaining obstacles are then set out: feedstock variability, phenolic inhibition, strain safety, scale-up, product stability, regulatory demands and economics. The data show grapevine waste as a versatile and valuable fermentation substrate and identify the reasons why laboratory results have not yet reached industrial scale.

Keywords: grapevine waste; grape pomace; solid-state fermentation; bioactive compounds; phenolic biotransformation; circular biorefinery; bioprocess engineering

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1. Introduction

Lignocellulosic residues pile up in the agri-food sector faster than they can be absorbed. Disposing of them carries an environmental cost and discards material that still holds usable chemistry [1]. Viticulture illustrates the point clearly. Pruning wood, canes, pomace, seeds, skins, lees and leaves return every season, in large volumes and in very different physical forms. Among them, pomace—the solid fraction left after pressing—dominates in most wine-producing regions. Circular bioeconomy thinking asks that such streams be treated as feedstock rather than as refuse: recover the molecules first, then the fiber, and send as little as possible to landfill or open burning [2–5].

Part of what makes these residues interesting is how chemically crowded they are. Phenolic acids, flavonoids, anthocyanins, tannins and stilbenes sit alongside dietary fiber, structural polysaccharides, lignin, proteins, minerals and seed oils. The

proportions shift constantly. Cultivar, climate, vineyard management, harvest ripeness, vinification protocol and the specific fraction sampled all leave their mark, which is why two pomace batches from neighboring cellars rarely behave the same way. That same heterogeneity underpins the wide biological profile reported for grape-derived extracts—antioxidant, antimicrobial and anti-inflammatory effects, together with useful technological properties—and explains their appeal to the food, nutraceutical, cosmetic, pharmaceutical and biomaterial industries.

Extraction practice has moved on considerably from conventional solvent maceration. Ultrasound- and microwave-assisted protocols, pressurized liquid and supercritical fluid systems, enzyme-assisted treatments and deep eutectic solvents are now used to target specific fractions instead of stripping everything at once. The motivation is partly analytical and partly economic: higher recovery of catechins, anthocyanins, resveratrol and viniferins, with less solvent, shorter runs and fewer downstream steps. What recent work adds is a warning against treating extraction in isolation. Purification, standardized analytical control and process optimization have to be designed together if the results are to hold up outside the laboratory [6–10].

Application routes differ according to which fraction is being handled. Polyphenol-rich extracts are being formulated as food ingredients and as natural preservatives or colorants. Seed-derived products and skin fractions are of interest to cosmetic formulators, while the lignocellulosic residue feeds into bio-based films, composites, adsorbents and energy carriers. Taken together, these routes trace a shift away from waste management toward integrated biorefining, in which each stream is used as fully as the process allows.

Several obstacles cut across all of these routes. Raw material composition varies from batch to batch, and extraction and analysis are still performed without common protocols, so published figures are difficult to compare. Economic and life cycle assessments remain partial. Regulatory approval for food and cosmetic uses is slow, and scale-up brings its own difficulties around solvent recovery, product stability and logistics. Until these are addressed, grapevine waste valorization will continue to advance faster in the literature than in industry [4,10–12].

This review takes fermentation as the central route through which grapevine waste acquires economic value. Solid-state and submerged bioconversion are examined in turn, with attention to how microbial activity releases bound phenolics and transforms them into different structures. The discussion then places these processes within circular biorefinery configurations and follows the sequence that determines whether a fermented product is viable at all—extraction, recovery, purification and industrial deployment—since consistency, safety and cost are decided along that chain rather than at any single step.

Several recent reviews have already examined grapevine and winery waste from the perspective of composition, extraction technology, or general circular bioeconomy strategy [1–5,13]. What distinguishes the present review is not the breadth of residues considered, which necessarily overlaps with this existing literature, but its explicit reframing of fermentation, rather than extraction, as the organizing axis: extraction, purification, and downstream processing are treated here as steps that condition and are conditioned by fermentation performance, rather than as an independent technology track summarized for its own sake. Concretely, this review (i) examines a study that compared solid-state and submerged fermentation on the same grape pomace substrate, with results expressed per gram of dry substrate, and states the limits of this single dataset; (ii) proposes, as a hypothesis derived from the general solid-state fermentation literature rather than as a demonstrated result, the process conditions under which

one fermentation mode may be expected to outperform the other; and (iii) integrates fermentation-based safety and detoxification evidence (notably for ochratoxin A) with the extraction and industrial-scale sections, which existing extraction-centered reviews of this residue stream do not attempt to the same degree.

Literature Search Strategy

In order to carry out the critical review, a structured literature search was conducted in Scopus, Web of Science (Clarivate), PubMed/MEDLINE, ScienceDirect, and Google Scholar, including all publications from January 2015 up to August 2026; particular emphasis was placed on studies published in the most recent five-year period (2021–2026) in order to obtain the latest available evidence on quantitative and technological processes. Where earlier studies were foundational or had a high citation count and still served as the main reference for a particular compound class, mechanism, or extraction method, they were included. The search strings linked terms relating to the raw materials ("grape pomace", "grapevine waste", "winery by-products", "vine pruning residues", "wine lees") with terms relating to the process or outcome of interest ("solid-state fermentation", "submerged fermentation", "microbial bioconversion", "extraction", "bioactive compounds", "phenolic compounds", "valorization", "circular bioeconomy"), using Boolean operators (AND/OR) and truncation where this was allowed by the database interface. AI-assisted tools (see Acknowledgments) were used to support execution of this search strategy, including database querying and reference verification; all final inclusion/exclusion decisions were made by the human authors.

Inclusion criteria required that a source be a peer-reviewed original research article, review, or book chapter published in English, and that it report at least one of the following on grapevine- or winery-derived residues: (i) compositional or bioactive compound data; (ii) an extraction, purification, or analytical method with a quantifiable outcome (yield, recovery, or activity); (iii) a fermentation process (solid-state, submerged, or lactic acid bacteria) with a reported product, titer, or enzymatic activity; or (iv) a safety, regulatory, techno-economic, or life cycle assessment relevant to any of the above. Priority was given to studies reporting quantitative results (yields, fold changes, titers, enzymatic activities, or percentage reductions) that could be compared across studies. Exclusion criteria comprised non-peer-reviewed sources (preprints not subsequently published, conference abstracts without full data, and the gray literature), studies on non-grapevine biomass used only as generic comparators, and duplicate reports of the same dataset. Because the field is large and mature, reference lists of retrieved reviews were additionally hand-searched to identify further primary studies not returned by the original search strings, and searches were periodically re-run with narrower, topic-specific term combinations (e.g., "solid-state fermentation" AND "grape pomace" AND "enzyme") to verify that recent (2023–2026) studies on each sub-topic had been captured rather than relying solely on the broader initial query.

Figure 1 summarizes the paper's scope through interconnected routes within a circular biorefinery framework for grapevine waste.

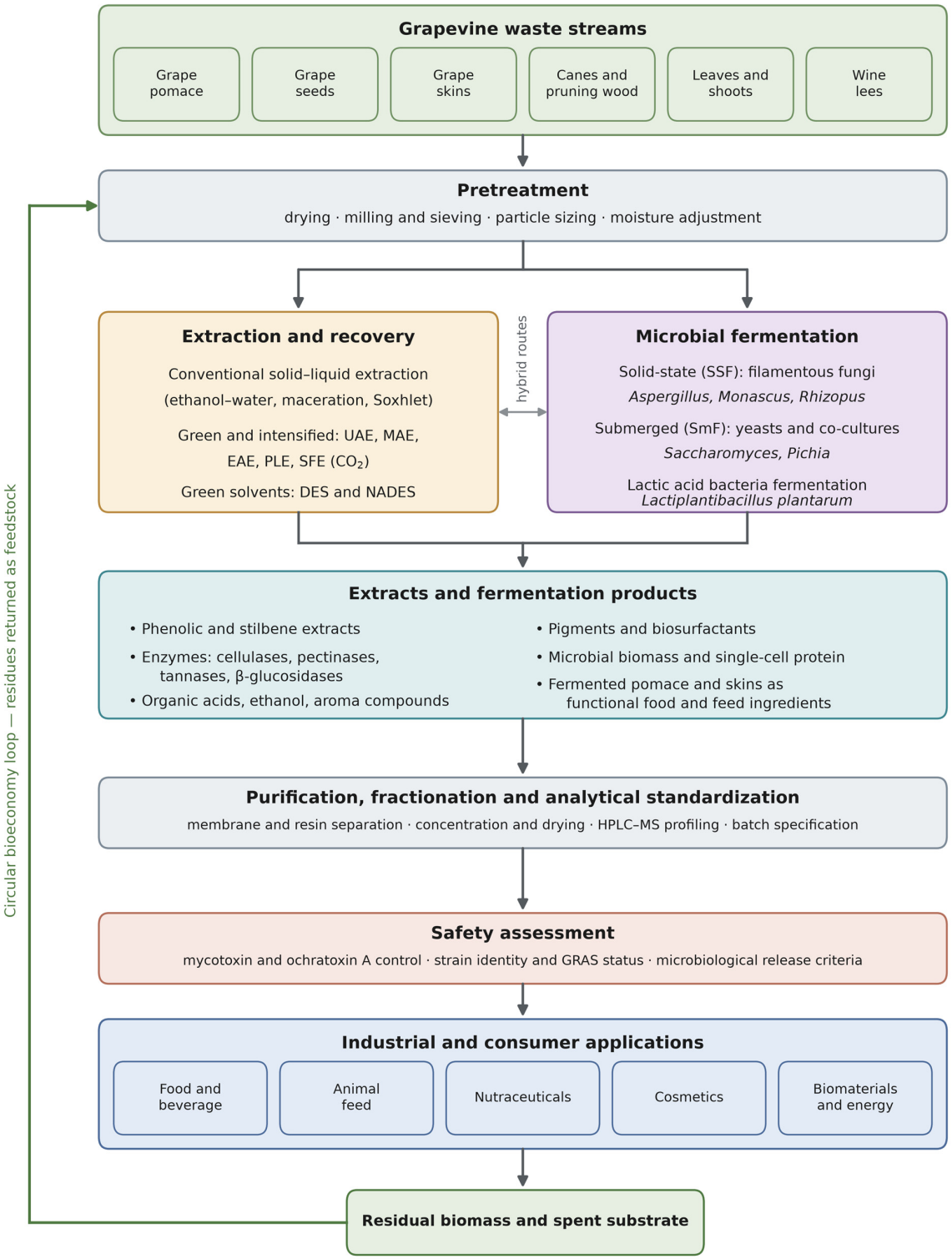


Figure 1. Overview of extraction- and fermentation-based processes for the valorization of grapevine waste. Residues (pomace, seeds, skins, canes and pruning wood, leaves, wine lees) are pretreated and then directed to conventional or green extraction and/or to solid-state, submerged or lactic acid bacteria fermentation; hybrid and sequential combinations of the two routes are also used. The resulting extracts and fermentation products are purified, analyzed, and standardized, then assessed for safety—including mycotoxin and ochratoxin A control and strain identity—before industrial and consumer use. Residual biomass re-enters the process as feedstock, closing the circular bioeconomy loop. SSF, solid-state fermentation; SmF, submerged fermentation; UAE, ultrasound-assisted extraction; MAE, microwave-assisted extraction; EAE, enzyme-assisted extraction; PLE, pressurized liquid extraction; SFE, supercritical fluid extraction; DES/NADES, (natural) deep eutectic solvents.

2. Fermentation-Based Valorization of Grapevine Waste

Fermentation-based valorization is a promising method to convert grapevine residues into higher-value ingredients, metabolites, and bioproducts, complementing extraction-centered strategies. While simple extraction recovers compounds already present in the biomass, microbial and enzymatic fermentation transforms the matrix itself: it releases phenolic compounds, fibers, reduces antinutritional or inhibitory compounds, and generates new metabolites with technological or biological relevance [13]. In this case, a biotransformation is possible. This depends on the type of microbial strain and the substrate. The degree of degradation is an important factor that could have an influence on the fermentation yield. Eukaryotic microorganisms (yeasts) are among the most active strains. Grape residues and wine lees supply carbon sources, minerals, residual sugars, phenolic substrates, and lignocellulosic fractions that can sustain microbial growth under solid-state or submerged conditions. Recent quantitative studies now allow direct comparisons of specific process configurations, strains, and yields. The field has moved beyond general statements about fermentation potential [14–19].

2.1. Microbial Platforms for Grapevine Waste Bioconversion

Filamentous fungi (Aspergillus, Monascus, Eurotium, Rhizopus, Pleurotus, Phanerochaete, and Bjerkandera) are used for solid substrate bioconversion because they are capable of secreting extracellular hydrolases, including cellulases, hemicellulases, pectinases, tannases, laccases, and β-glucosidases. They are capable of depolymerizing lignocellulosic and tannin-rich complexes [20]. Yeasts, including *Saccharomyces cerevisiae* and non-*Saccharomyces species* such as *Pichia stipitis*, are relevant for residual sugars or hydrolysates are available, and their sequential or simultaneous use with filamentous fungi in co-culture has been shown to substantially increase phenolic and flavonoid yields relative to monocultures [21]. Lactic acid bacteria, notably *Lactiplantibacillus plantarum* and related species, are a versatile bacterial strain chosen for food-oriented fermentation because they acidify the substrate, are generally recognized as safe (GRAS), and transform the phenolic profile while generating organic acids and exopolysaccharides [22]. Among these, *Aspergillus* and *Rhizopus* species have the most established track record on grape pomace specifically, each supported by multiple independent studies with converging results; *Monascus*, *Eurotium*, and white-rot genera such as *Trametes* have so far been reported in a single or a small number of grape pomace-specific studies each, and their performance relative to the better-studied genera should accordingly be read as promising rather than confirmed.

2.2. Solid-State Fermentation: Mechanisms and Quantitative Evidence

Solid-state fermentation (SSF) is an optimal fermentation mode for grape and pomace seeds because it is a substrate-limited fermentation process. These factors are determined by the limited water content, necessary carbohydrates, and residual nutrients. In this situation, the type of fermentator is relevant to high yield based on the bioconversion rate. Recent quantitative studies provide concrete criteria for evaluating the impact of this effect. Fungal SSF of grape pomace seeds with *Aspergillus niger*, *Monascus anka*, and *Eurotium cristatum* (28 °C, 65% relative humidity, 12 days) increased the soluble total phenolic content up to 6.42-fold and total flavonoid content up to 6.68-fold relative to unfermented seeds. In parallel increases in DPPH (2.14-fold) and ABTS (3.64-fold) radical scavenging activity, the increase was strongly correlated with glycosidase activity (r = 0.900) and was accompanied by significant rises in several individual phenolics, notably resveratrol, epicatechin gallate, and phenolic acids such as ferulic, syringic, and chlorogenic acid [19]. Fermentation of grape pomace with *Rhizopus oryzae* was performed in both laboratory jars and an industrial

bioreactor over 15 days. It produced reproducible results in phenolic profile and chemical composition after the fungal enzymatic activity. All of these support the feasibility of scale-up beyond flask level [23]. Co-culture SSF that combined *Pichia stipitis* (yeast) with *Aspergillus niger* GH1 achieved considerably higher titers than either monoculture, with maximum yields of 62.46 g/L total flavonoids and 32.04 g/L condensed tannins after 120 h, alongside an expanded profile of 38 identified phenolic compounds, illustrating that microbial interaction in co-culture can be exploited deliberately as a process variable rather than treated as an uncontrolled artifact [21]. Two additional, independently conducted SSF studies on grape pomace support this general pattern with different fungal species and target products: solid-state fermentation with the white-rot fungus *Trametes versicolor* over 15 days increased the extractability of 13 individual phenolic compounds while simultaneously raising the ash, crude protein, and free fat content by up to 28–29%, 10–11%, and 7–17%, respectively, with laccase and xylanase activities reaching 2.66 and 346.04 U/g dry biomass in laboratory jars; and co-cultivation of *Trametes villosa* and *Trichoderma asperellum* on a grape pomace–wheat bran mixture yielded β-glucosidase, xylanase, β-xylosidase, and laccase activities of up to 218.91, 170.28, 19.39, and 16.5 U per gram of dry solid substrate, respectively [24,25]. Taken together with the co-culture and monoculture results above, these independent studies indicate that the magnitude of the SSF advantage is species- and enzyme-specific, but that a positive effect on either phenolic extractability or hydrolytic enzyme titer, relative to unfermented or non-optimized controls, has now been reported across at least four distinct fungal systems on grape pomace.

From an industrial perspective, this type of fermentation offers many benefits for grapevine waste processing: it operates with relatively low water demand and is compatible with many of the agro-industrial residues. It concentrates enzyme activity directly within the solid matrix [3]. However, SSF scale-up calls for careful control of thermal differences, aeration, moisture content, oxygen transfer, particle size, and inoculum distribution, and contamination risk increases with batch size; the transition from laboratory trays or flasks to pilot and industrial bioreactors is still a key bottleneck for reproducible product quality [19,23].

2.3. Solid-State Versus Submerged Fermentation: A Direct Comparison

A major deficiency in many papers based on grapevine waste valorization is the lack of head-to-head process comparison. One study compared SSF, semi-liquid fermentation and submerged fermentation (SmF) on the same dried red grape pomace (4 g dry substrate per flask, 0.04 g/mL in SmF), using *Pleurotus ostreatus* and *P. pulmonarius* for 20 days and expressing biomass and enzyme activities per gram of dry substrate [26]. Laccase activity was higher under SSF than under SmF (26,247 vs. 4447 U/g dry substrate for *P. ostreatus*, approximately 5.9-fold; 15,273 vs. 12,174 U/g for *P. pulmonarius*, approximately 1.3-fold), whereas endoglucanase activity (0.93 vs. 0.05–0.07 U/g dry substrate for *P. ostreatus*, i.e., more than 13-fold) and fungal biomass (0.50–0.54 g/g dry substrate) peaked under SmF; the total phenolic content decreased by 68–79% in all fermentation modes [26]. Studies of this type are important for translating laboratory yields into defensible process selection criteria for industry, because SSF and SmF differ systematically in water demand, oxygen transfer, achievable titers, and downstream separation requirements (Table 1). This scarcity of direct comparisons is a genuine limitation of the present evidence base, and the considerations below, which are taken from the general SSF literature on lignocellulosic agro-industrial substrates, should therefore be read as a working hypothesis rather than as evidence of a difference between the two fermentation modes on grapevine waste.

On the basis of the general SSF literature on lignocellulosic agro-industrial residues, the following hypothesis can be formulated; it has not yet been tested on grapevine waste. SSF may be expected to outperform SmF when (i) the substrate is a solid lignocellulosic

matrix containing little or no free water, such as grape pomace (or pruning wood after moisture conditioning), that filamentous fungi can colonize without submersion; (ii) the absence of a free liquid phase is itself desirable, since it simultaneously reduces the risk of bacterial contamination and lowers the energy demand associated with subsequent drying or dewatering; and (iii) the target product is an extracellular hydrolytic enzyme or a metabolite whose concentration benefits from the high local substrate-to-water ratio achieved in the solid matrix, which has repeatedly been associated with higher volumetric enzyme titers, lower energy requirements, and reduced wastewater generation compared with SmF on equivalent lignocellulosic feedstocks [27]. Conversely, SmF would be expected to remain preferable when homogeneous mixing, precise on-line control of pH, dissolved oxygen, and temperature are required, when the organism or product requires a genuinely liquid environment, such as free bacterial or yeast cells producing organic acids or biosurfactants, or when the production line must rely on the stirred-tank infrastructure and scale-up expertise already established for most industrial fermentations, since SSF bioreactor design remains comparatively less mature at pilot and industrial scale. Grape pomace, a moist solid with little free water, fits the profile under which SSF is hypothesized to perform best, and the higher laccase activity obtained under SSF in [26] is consistent with this hypothesis; the higher endoglucanase activity obtained under SmF in the same study shows, however, that the outcome depends on the target enzyme. A single study cannot confirm the hypothesis, and matched, grapevine waste-specific comparisons covering other organisms and products are required before a general advantage of either fermentation mode can be claimed. In practical terms, and summarized in Table 1, these considerations reduce to three decision criteria for grapevine waste bioprocessing: (i) choose SSF when the feedstock is a moist, low-free-water solid (grape pomace or moisture-conditioned canes) and the target output is an extracellular hydrolase or a phenolic-/flavonoid-enriched solid fraction, since every fungal system tested to date on grape pomace under SSF—spanning four distinct species or co-cultures [19,21,23,26]—has reported a positive effect on at least one of these outputs; (ii) choose SmF when the product must accumulate in a genuinely liquid phase (organic acids, biosurfactants, free microbial biomass, or an enzyme recovered in solution) or when tight on-line control of pH, dissolved oxygen, and temperature is required; and (iii) treat the magnitude of any reported advantage as organism- and product-specific rather than general, since the only matched, same-substrate comparison available [26] found SSF favored one enzyme (laccase) while SmF favored another (endoglucanase) and achieved higher biomass.

Table 1. Comparative overview of solid-state (SSF) and submerged (SmF) fermentation strategies for grapevine waste valorization, with quantitative outcomes.

Parameter	Solid-State Fermentation (SSF)	Submerged Fermentation (SmF)
Typical substrate form	Moist solid pomace or pomace seeds; low free water	Pomace hydrolysate, wine lees extract, or liquid medium
Representative microorganisms	*Aspergillus niger*, *Monascus anka*, *Eurotium cristatum*, *Rhizopus oryzae*, *Pichia stipitis* (co-culture) [19,21,23]	Bacterial, LAB, and yeast platforms in liquid hydrolysate; *Pleurotus ostreatus* and *P. pulmonarius* compared directly with SSF on identical substrate [26]
Representative quantitative outcome	TPC +6.42×, TFC +6.68×, DPPH +2.14×, ABTS +3.64× (12 d, 28 °C, 65% RH) [19]; 62.46 g/L total flavonoids, 32.04 g/L condensed tannins after 120 h co-culture [21]; on matched substrate, laccase 26,247 U/g dry substrate (*P. ostreatus*) and 15,273 U/g dry substrate (*P. pulmonarius*), endoglucanase 0.05–0.07 U/g dry substrate [26]	On the same matched substrate, laccase 4447 U/g dry substrate (*P. ostreatus*; approximately 5.9-fold lower than under SSF) and 12,174 U/g dry substrate (*P. pulmonarius*; approximately 1.3-fold lower), but endoglucanase up to 0.93 U/g dry substrate (more than 13-fold higher than under SSF) and the highest fungal biomass (0.50–0.54 g/g dry substrate) [26]; independently, shake flask SmF with Bacillus subtilis natto on grape pomace hydrolysate achieved 0.176–0.178 IU/mL cellulase activity [28] (bacterial enzyme expressed in volumetric units; not comparable with the fungal SSF data in the adjacent column)

Table 1. *Cont.*

Parameter	Solid-State Fermentation (SSF)	Submerged Fermentation (SmF)
Water/energy demand	Low free water requirement; lower energy for downstream drying	Higher water demand; requires acid or enzymatic hydrolysis pretreatment
Main scale-up bottleneck	Heat and moisture gradients, aeration, and mixing in solid bed bioreactors	Bioreactor mixing costs and phenolic inhibition of microbial growth at high substrate loads
Best-suited outputs	Enzyme-enriched substrates, antioxidant-rich fermented pomace, fiber-modified ingredients	Organic acids, ethanol, microbial biomass, and enzymes recovered in solution

Figure 2 summarizes these considerations as a hypothesis-based decision pathway for selecting between SSF and SmF on grapevine-waste substrates, making explicit that the current evidence supports a substrate- and product-specific recommendation rather than a universal ranking of one fermentation mode over the other.

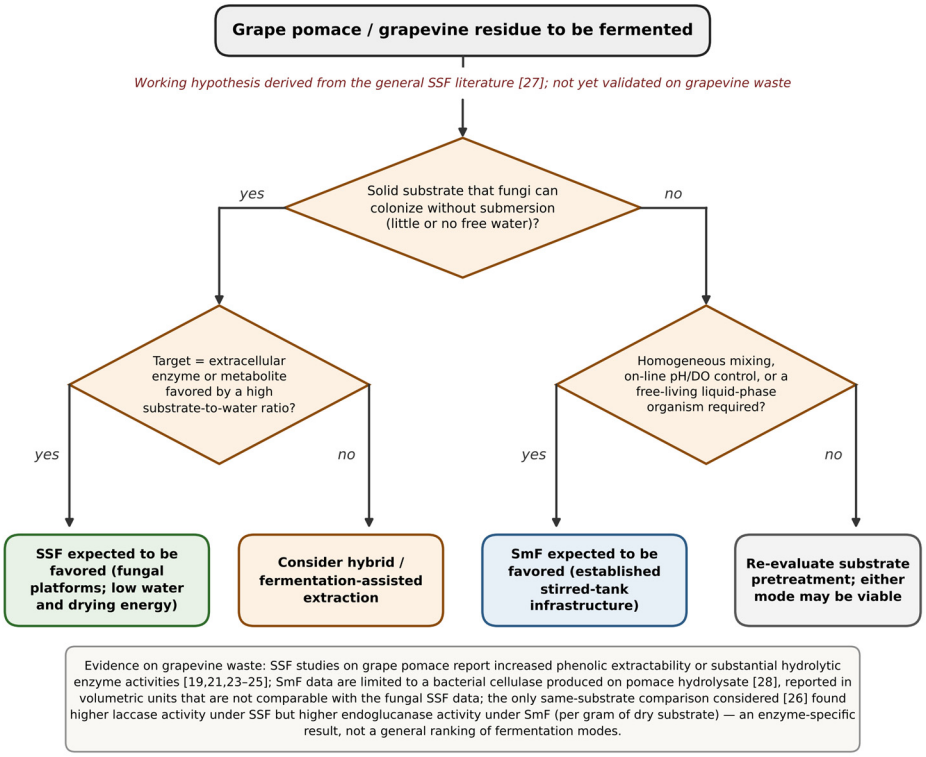


Figure 2. Hypothesis-based decision pathway for selecting solid-state (SSF) versus submerged (SmF) fermentation of grapevine waste, based on substrate physical form and target product requirements. The pathway is derived from the general SSF literature [27] and has not been validated on grapevine waste. The supporting evidence box lists the specific quantitative studies underlying each branch and explicitly flags that the only matched, same-substrate comparison available [26] is enzyme-specific (laccase favored by SSF, endoglucanase by SmF) rather than generalizable to all fermentation outputs.

2.4. Submerged Fermentation and Production of Value-Added Metabolites

Submerged fermentation is relevant in the case of grape pomace hydrolysates, wine lees extracts, or soluble sugar-rich fractions being used as liquid fermentation media. These media support the production of organic acids, ethanol, enzymes, microbial biomass, biosurfactants, and pigments depending on the organism and nutrient supplementation. Because SmF requires a pretreatment phase, dilute acid or enzymatic hydrolysis is necessary to solubilize the lignocellulosic fraction. The whole process depends on the hydrolysis intensity. The presence of phenolic compounds in the liquid medium can restrain microbial growth at elevated concentrations. Dilution, pH adjustment, detoxification, and different processing phases, in which high-value phenolics are recovered first, and the residual

carbohydrate-rich stream is subsequently fermented, are the main mitigation strategies analyzed in the recent database-indexed literature [2,19]. An independent submerged fermentation study on grape pomace hydrolysate provides a further, bacterium-based data point: shake flask cultivation of *Bacillus subtilis* natto DSM 17766 on acid-pretreated grape pomace hydrolysate, optimized by response surface methodology, achieved a maximum cellulase activity of 0.176–0.178 IU/mL at a solid-to-liquid ratio of 15:100 (w/v), pH 6.0, after 7 days, with the fermentation period and pH exerting a stronger effect on activity than the amount of grape pomace used [28]. Because this value refers to a different enzyme, produced by a bacterium and expressed in volumetric units (IU/mL), it cannot be compared with the fungal laccase, xylanase and β-glucosidase activities expressed per gram of dry substrate in Section 2.2, and it does not demonstrate a yield difference between the two fermentation modes.

2.5. Lactic Acid Bacteria Fermentation and Functional Food Ingredients

In the last decade, LAB fermentation technology of grape pomace has moved from proof of concept toward strain-level process development. This shift reflects genuine industrial demand for food-grade, GRAS-compatible fermentation routes rather than laboratory proof of concept alone. Based on a substrate optimization study, grape pomace presence in the media above 10% (*w*/*v*) determined a reduced LAB viability by up to two log unless pH was corrected. The pomace fraction had to be lowered to 2.5–5% with carbon/nitrogen supplementation to sustain fermentation. Screening of eleven LAB strains identified *Lactiplantibacillus plantarum* T0A10 as the best-performing strain, and the resulting sourdough containing 5% grape pomace showed high DPPH and ABTS radical scavenging activity together with anti-inflammatory potential in Caco-2 cells, as well as a qualitatively and quantitatively modified anthocyanin profile [22]. These findings provide transferable operating parameters in the industrial sectors. They are based on substrate load, strain selection, and pH control, for scaling grape pomace LAB fermentation toward bakery or functional ingredient applications.

2.6. Fermentation-Assisted Recovery and Bioavailability of Phenolic Compounds

Fermentation-assisted recovery is relevant for grapevine residues because a considerable fraction of phenolics is not free in residues. It is associated in substrates with cell wall polysaccharides, proteins, tannins, or other insoluble matrices. Microbial enzymes hydrolyze glycosidic bonds, ester linkages, and polysaccharides, increasing soluble phenolic concentrations and strongly changing the extract's qualitative profile. This is important not only for the extraction yield but for bioaccessibility and biological activity. Fermentation may increase the proportion of low-molecular-weight phenolics that are more readily released during digestion or further transformed by gut microbiota. In addition, microbial metabolism can reduce bitterness, astringency, or instability in some fractions, although excessive degradation of anthocyanins, stilbenes, or tannins is a risk if the fermentation conditions are not controlled [19,21].

Fermentation works on two levels: as a bioconversion route in its own right and as a pretreatment that makes subsequent extraction easier. Coupled with ultrasound, enzyme-assisted extraction, membrane separation, resin adsorption or green solvents, it can improve selectivity and reduce dependence on the more costly of these techniques. What limits its use is standardization. An ingredient destined for food, nutraceutical, cosmetic or pharmaceutical use cannot be described by the total phenolic content and antioxidant activity alone; it also needs defined target compounds, a known residual microbial load, evidence that mycotoxins are absent, control of solvent residues and allergen risk, and demonstrable consistency from batch to batch.

2.7. Target Products and Functional Outcomes

The products obtained from grapevine waste fermentation fall into a few functional groups. Enzymes are the most direct route: cellulases, hemicellulases, pectinases, tannases and β-glucosidases can either be recovered and sold as industrial preparations or left to act in situ, improving phenolic release and fiber breakdown in the substrate itself. Microbial metabolism yields a second group, namely organic acids, ethanol, aroma compounds, pigments, biosurfactants and the biomass as such, with the profile depending on the organism and the fermentation mode. A third group covers fermented pomace and skins used directly as functional ingredients in food, feed, bakery products, nutraceuticals or cosmetics, provided that safety, sensory quality and compositional reproducibility can be shown [29]. Bioprocessing studies published recently report that fermentation of grape pomace markedly raises the soluble phenolic content and antioxidant capacity relative to the untreated substrate, improves dough and bakery performance, and points toward circular food ingredients with anti-inflammatory potential [19,21,22].

2.8. Safety, Mycotoxin Control

Safety and standardization are decisive for translating fermentation-based valorization into food, feed, cosmetic, or nutraceutical products. Grape pomace is a documented risk matrix for ochratoxin A (OTA), produced mainly by several well-known strains, like *Aspergillus carbonarius*, *A. ochraceus*, and related *Aspergillus* and *Penicillium* species during ripening, harvest, or storage, especially; the European Union sets a maximum OTA level in wine and applies limits to dried vine fruits and processed cereal-derived food products, with risk assessments periodically updated by the European Food Safety Authority (EFSA). Fermentation itself can form part of the safety solution: pressure cooking alone reduced OTA by approximately 33–35%, whereas the same treatment combined with 24 h LAB fermentation with *Lactiplantibacillus plantarum*, *Lacticaseibacillus paracasei*, or *Lactobacillus acidophilus* reduced the OTA content in contaminated grape pomace by up to 97%, with acidification, microbial competition, and production of antifungal organic acids proposed as the main mechanisms. Strain choice was decisive, since *Lactobacillus bulgaricus* achieved only 45% OTA reduction even after 72 h [30]. These results show that LAB fermentation should be regarded not only as a bioconversion tool but as a functional detoxification step, although the fate and residual toxicity of OTA degradation products (e.g., ochratoxin α) remain incompletely characterized and warrant quantification in future work [30]. Beyond OTA, filamentous fungal SSF requires particular attention because enzyme production and phenolic release must be achieved without triggering mycotoxin formation by the same genera (Aspergillus, Penicillium) that are used as bioconversion agents; strain confirmation, absence of toxin testing, and batch-to-batch microbiological release criteria are critical elements for any industrial fermentation protocol based on grapevine waste.

2.9. Industrial Integration and Future Research Targets

It is important to state explicitly the technology readiness level of the evidence reviewed above before discussing industrial integration. With the partial exception of the tray bioreactor and pilot-scale ultrasound extraction studies cited in Sections 2.2 and 5, essentially all of the fermentation yields, titers, and enzyme activities reported in this review, including those in Table 1, were obtained at laboratory scale (flasks, jars, or bench-top bioreactors of a few liters), typically under controlled, single-batch conditions and with grape pomace sourced from one or a few cultivars and vintages. "Industrial relevance" and "industrial potential," as used throughout this review, should therefore be read as an assessment of technical compatibility with anticipated industrial constraints (substrate availability, equipment familiarity, regulatory pathway), not as evidence that a given fer-

mentation route has been demonstrated at pilot or industrial scale. To our knowledge, no published study has yet reported solid-state or submerged fermentation of grapevine waste at a throughput exceeding a few kilograms of substrate per batch with continuous or semi-continuous operation, and techno-economic and life cycle data specific to fermentation (as opposed to extraction; see Section 5.6) remain scarce and, where available, derive from process design models rather than from operating plants (see the last paragraph of this section). Closing this laboratory-to-pilot gap, rather than further optimizing laboratory-scale yields, is arguably the single highest-priority need for translating the fermentation routes reviewed here into operating industrial processes.

For industrial implementation, fermentation technology should be integrated with existing winery and biorefinery infrastructure, rather than being treated as an isolated process confined to individual local producers. Potential models include on-site stabilization and fermentation of fresh pomace, regional collection hubs in order to obtain standardized substrate processing, co-processing of pomace with other fruit residues, and combined extraction–fermentation–material recovery chains [31]. Wine lees are particularly interesting because they already originate from fermentation and contain yeast biomass, mannoproteins, β-glucans, tartrates, and adsorbed phenolics that may be recovered or further biotransformed [32]. Similarly, pruning wood and canes may be used after pretreatment as lignocellulosic substrates for enzyme production or as residual material after stilbene extraction.

Future studies should prioritize pilot-scale validation with matched substrates and standardized reporting [26]. Microbial strain selection should be based on several data points: substrate variability, minimum carbon and nitrogen source levels, process modeling data, techno-economic assessment, life cycle analysis, and a deep evaluation of fermented products during the entire process. Particular attention should be given to safety when filamentous fungi are used, including strain identity, absence of toxin production, and compliance with food or feed regulations, building on the quantitative detoxification benchmarks already reported for LAB fermentation of ochratoxin A-contaminated pomace [30]. Fermentation expands the valorization potential of grapevine waste by transforming residues into real functional ingredients, enzymes, metabolites, and stabilized biomaterials. These considerations are in concordance with EU regulatory directives [33].

Sustainability assessments of fermentation routes for grapevine waste are few and represent a priority gap for this field. The most complete example is a combined TEA and LCA of a biorefinery processing the three main winery waste streams (grape pomace, stalks and wine lees), in which a phenolic-rich extract, grape seed oil, calcium tartrate and a tannin-rich extract were recovered and succinic acid was produced by fermentation [34]. The minimum selling price of succinic acid was estimated at USD 1.23–2.76/kg, depending on the market price and end-use of the co-products, with a global warming potential of 1.47 kg CO_2-eq and an abiotic depletion potential of 25.2 MJ per kg of dry waste [34]. These values were obtained from process design and estimated mass and energy balances rather than from an operating plant, and they refer to submerged succinic acid production rather than to the solid-state or lactic acid bacteria routes that dominate the studies reviewed here; they cannot therefore be transferred directly to those routes, although the study provides a methodological template for assessing them. Life cycle assessment (LCA), following the ISO 14040/14044 framework, allows a direct comparison of the environmental burden of SSF- and SmF-based valorization routes. This can be compared with conventional disposal routes, which include: landfilling, composting, or incineration, or extraction-only pathways, accounting for energy use in aeration, mixing, heating, and downstream drying or purification. A techno-economic assessment (TEA), typically expressed by means of metrics such as minimum selling price, net present value, and internal rate of return, is needed to determine whether the value of

fermentation-derived products (enzymes, organic acids, enriched extracts) offsets capital and operating costs at pilot and industrial scale. Very few of the studies reviewed here report the raw process data (energy input, water consumption, yield per unit of feedstock) required to populate such models, and subsequent studies should explicitly capture this information alongside compositional and bioactivity outcomes so that LCA and TEA can be conducted retrospectively across the literature rather than requiring dedicated new studies. Embedding sustainability metrics into standards would also allow fermentation routes to be compared directly with extraction-based approaches [34,35]. Hybrid strategies were examined throughout this paper as an evidence base for industrial adoption within a genuinely circular biorefinery model.

3. Types and Sources of Grapevine Waste

Grapevine waste comes from both vineyard management and winery activities, and the type and quantity produced are strongly influenced by the stage in the production process. Generally, the residues can be split into those produced during pruning and industrial process management, and the by-products obtained during crushing, fermentation, and sedimentation in the winemaking industry. The origin of the residue strongly affects the moisture content, lignocellulosic composition, bioactive compound levels, seasonality, and logistics across all stages [36]. The grape pomace is the main end product after vinification, while pruning residues are the most abundant lignocellulosic fraction produced each year as a result of all the processes [2,4,37]. In quantitative terms, pomace corresponds to approximately 20–30% of the mass of processed grapes, consists of roughly 50% skins, 25% seeds and 25% stalks, and is generated at about 9 million tons per year worldwide [4,10]; wine lees account for about 5% of the grape mass [36], and pruning wood is produced at 1–5 t per hectare per year [6].

The most relevant substrates include pruning wood, canes, shoots, leaves, and, in some production systems, thinned bunches. These substrates are generated seasonally during winter pruning, summer canopy control, and vineyard renewal practices. Pruning wood and canes are especially important because they are produced in high volumes and are rich in structural polysaccharides, lignin, and stilbene-type compounds such as resveratrol and viniferins. Leaves and green shoots are studied at large-scale, low-level extraction, but they may contain phenolic compounds and could serve as promising feedstocks for specific uses where local collection is possible [6–8,37,38].

Grape wastes account for most of the secondary products a winery generates. Pomace, that is skins and seeds together with stems and residual pulp when these are not separated during processing, makes up the bulk of the solid residue and is the fraction whose polyphenols have been studied most. Seeds interest the food industry because of their flavan-3-ols, proanthocyanidins and oil content, while skins carry the anthocyanins, flavonols and much of the dietary fiber. Lees, which settle during fermentation and storage, consist largely of yeast biomass, tartrate salts and compounds derived from them, and offer a further, less exploited route to recovery and bioprocessing [4,11,32,36,37,39–42]. Quantitatively, winery yeast lees have been reported to contain 12.2–26.1% dry matter, with the dry fraction comprising 32.6–46.0% protein and 19.2–24.6% carbohydrates depending on the vinification technology, while ultrasound-assisted β-glucan extraction yields of 19.0–39.4% (autolysis) or 3.5–19.8% (acid–base hydrolysis) have been achieved depending on the recovery method and yeast origin, illustrating that lees composition is itself a function of upstream winemaking choices and not a fixed property of the residue [43].

Because these streams differ so much, they call for different handling. Wet, phenolic-rich residues such as pomace and lees are usually processed for antioxidants and functional ingredients. Dry lignocellulosic fractions, such as canes and pruning wood, lend themselves instead

to stilbene recovery and to bio-based products, adsorbents or energy uses. Sorting grapevine waste by origin and composition is therefore a practical prerequisite for the pretreatment, extraction and processing routes discussed in the sections that follow [2,10,37,44]. This distinction matters specifically for fermentation, the central focus of this review: wet, phenolic-rich pomace and lees are the substrates on which Section 2 concentrates because their moisture and nutrient profile directly support microbial growth, whereas dry canes and pruning wood are treated in Sections 3–5 primarily as an extraction feedstock precisely because their low moisture content makes them comparatively poor solid-state fermentation substrates without additional conditioning.

4. Chemical Composition and Bioactive Profile

How much industrial value a grapevine residue holds depends on what it is made of: a polymeric matrix plus a wide range of extractable bioactives. Across the main residue types, these include phenolic acids, flavonoids, anthocyanins, flavan-3-ols, proanthocyanidins, stilbenes, organic acids, dietary fiber, lignin, cellulose, hemicellulose, lipids, proteins and minerals. The distribution is far from uniform. Pomace, seeds and skins hold the more readily extractable phenolics, whereas canes and pruning wood are the better sources of stilbenes and of lignocellulose.

Seeds are rich in flavan monomers and polymeric proanthocyanidins, and their lipid fraction is high in unsaturated fatty acids. Skins supply anthocyanins, flavonols, phenolic acids and insoluble fiber. Pomace contains most of these compounds, though in proportions that shift with the processing route. Its phenolic load after pressing and fermentation is high enough to explain why it has become the residue of choice for extracting functional ingredients. Pomace also carries adsorbed phenolics, yeast-derived molecules and tartrate-associated material, all of them sensitive to fermentation and storage conditions. Quantitatively, in six red cultivars analyzed over two vintages, the total phenolic content ranged from 36.6 to 88.7 mg gallic acid equivalents (GAE)/g dry weight (DW) in the seeds of fresh grapes and from 12.6 to 44.5 mg GAE/g DW in the seeds recovered from the corresponding pomace, whereas skins contained 20.2–52.3 mg GAE/g DW before and 11.8–31.6 mg GAE/g DW after vinification [45].

Vineyard residues, namely canes, shoots and pruning wood, have a composition of their own: lignocellulosic, and marked by stilbene-type phytoalexins such as *trans*-resveratrol, ε-viniferin and related oligomers, which are of interest for their antioxidant and antimicrobial activity. Cellulose, hemicellulose and lignin occur in proportions that matter for bio-based materials and other non-food uses. Leaves and young shoots add flavonoids, phenolic acids and pigments, but they remain the least standardized feedstock, since availability depends on agronomic practice and on how collection is organized. Reported concentrations illustrate the magnitude of this resource: optimized microwave-assisted solvent extraction from pruning wood has yielded 0.77–0.81 mg/g DW of *trans*-resveratrol and 1.36–1.40 mg/g DW of ε-viniferin, while on grape cane, accelerated solvent extraction in methanol has recovered as much as 6.03 mg/g DW of *trans*-resveratrol and extraction at 50 up to 2.26 mg/g DW of ε-viniferin, underscoring both the abundance of this resource and the strong dependence of the recoverable stilbene content on the extraction protocol used [6,8].

Compositional variability is a persistent obstacle for both research and industrial use. Cultivation practice, site, climate, ripening stage, the type of vinification (red or white), the fermentation itself, drying and length of storage all affect how much of a given compound is present and how stable it remains. Recent work has therefore pushed for standardized analytical protocols, targeted phenolic profiling and clearer links between composition and measured biological activity. Without these, it is difficult to decide which residue

stream suits which application: polyphenol-rich extracts, dietary fiber, stilbene fractions, or lignocellulosic feedstock for bio-based products [4,6,40,46]. These compositional differences are not merely descriptive: the same properties that determine which extraction route suits a given residue (Section 5) also determine its suitability as a fermentation substrate (Section 2)—high moisture and residual sugar content favor microbial colonization and are therefore prerequisites for the solid-state and lactic acid bacteria fermentation routes discussed later, while the lignocellulosic, low-moisture character of canes and pruning wood instead favors their use as an enzyme production substrate once combined with a moisture-conditioning pretreatment. Expressed on the same mg GAE/g DW basis, the ranges compiled in Table 2 show that grape seeds (up to ≈89 mg GAE/g DW) and skins (up to ≈52 mg GAE/g DW) are substantially richer in total phenolics than canes and pruning wood (10.6–32.6 mg GAE/g DW), which instead stand out as the principal stilbene-bearing fraction; leaves and wine lees are reported in the literature primarily through compound class-specific rather than aggregate TPC values, reflecting the comparatively narrower analytical focus these two fractions have received to date.

Table 2. Chemical composition and industrial significance of the primary grapevine waste fractions, with reported contents expressed on a dry weight (DW) basis and the amounts generated.

Residue Fraction	Dominant Compound Classes	Representative Compounds; Reported Contents (DW) and Amounts Generated	Principal Bioactivity/Industrial Relevance	References
Grape seeds	Flavan-3-ols, proanthocyanidins, seed lipids, tocopherols	Catechin, epicatechin, procyanidin B1/B2, linoleic acid; TPC 36.6–88.7 mg GAE/g DW (seeds of fresh grapes) and 12.6–44.5 mg GAE/g DW (pomace seeds); oil 8–20% (*w*/*w*); about 25% of pomace mass	Antioxidant, antimicrobial, nutraceutical, and food ingredient potential	[4,10,37,40,45]
Grape skins	Anthocyanins, flavonols, phenolic acids, insoluble dietary fiber	Malvidin-3-O-glucoside, quercetin derivatives, caftaric acid; TPC 20.2–52.3 mg GAE/g DW (fresh skins) and 11.8–31.6 mg GAE/g DW (pomace skins); about 50% of pomace mass	Natural colorant potential, antioxidant activity, and functional food applications	[4,40,41,45,46]
Grape pomace	Mixed phenolic fraction, tannins, anthocyanins, phenolic acids, dietary fiber, minerals	Gallic acid, catechins, procyanidins, anthocyanins, tartaric acid; TPC 38.5–50.0 mg GAE/g DW (enzyme-assisted and pressurized liquid extracts); 20–30% of processed grape mass, about 9 million t/year worldwide	Multifunctional substrate for extracts, food ingredients, cosmetics, and biomaterials	[2,4,10,14,39,47]
Canes/pruning wood	Stilbenes, lignin, cellulose, hemicellulose	*trans*-Resveratrol, ε-viniferin, piceid; *trans*-resveratrol 0.77–6.03 mg/g DW, ε-viniferin 1.36–2.26 mg/g DW; TPC 10.6–32.6 mg GAE/g DW (ultrasound-assisted extracts of canes); pruning wood 1–5 t/ha/year	Antioxidant and antimicrobial compounds; raw material for bio-based products	[6–8,12,38,48,49]
Leaves	Flavonoids, hydroxycinnamic acids, pigments	Quercetin, kaempferol, caffeic acid, chlorophylls, carotenoids; flavonols 19–42 mg/g DW, hydroxycinnamic acids 3.2–7.6 mg/g DW, flavan-3-ols 0.7–3.5 mg/g DW, chlorophyll a 0.25–2.50 mg/g DW (leaves sampled during the growing season)	Antioxidant potential and niche food, cosmetic, or pharmaceutical applications	[12,15]
Wine lees	Yeast-derived polysaccharides, β-glucans, mannoproteins, adsorbed phenolics, tartrates	β-Glucans, mannoproteins, tartaric salts; protein 32.6–46.0% and carbohydrates 19.2–24.6% of dry matter; β-glucan yield 3.5–39.4% of dry matter (ultrasound-assisted recovery, method-dependent); about 5% of grape mass	Functional ingredients, fermentation aids, and antioxidant-rich fractions	[4,16,32,36,43]

5. Extraction and Recovery Technologies of Bioactive Compounds from Grapevine Waste

Moving from composition to actual valorization comes down to how well the recovery step performs: how much it extracts, how selectively, and at what scale. The substrate makes this difficult. Moist pomace, oily seeds, pigmented skins, lignified canes and fermentation lees behave very differently, so no single protocol serves them all. The choice

has to match the target compounds and the physicochemical state of the raw material, and it has to anticipate what the extract will be used for. Practical constraints weigh just as heavily: solvent safety, energy demand and the purification steps that follow. Extraction is therefore best treated not as an isolated operation but as one link in a chain running from pretreatment through fractionation and stabilization to the final application [4,9,39,46,48].

5.1. Conventional Extraction Methods

Solid–liquid extraction is still the workhorse for recovering phenolics, pigments and other soluble constituents from pomace, seeds, skins, canes and lees. Hydroalcoholic mixtures, aqueous acetone or other polar organic solvents are chosen according to the polarity of the target compounds. Ethanol–water systems have found the widest acceptance, since they combine reasonable yields with low toxicity and raise few concerns in food, nutraceutical or cosmetic applications. Maceration and Soxhlet extraction persist mainly in analytical and comparative work, where reproducibility across laboratories matters more than throughput. Their drawbacks are well known: long extraction times, large solvent volumes and fixed temperatures, conditions under which thermolabile constituents such as anthocyanins and some stilbenes may oxidize or degrade [8,9,46].

Conventional extraction still matters, for at least three reasons:

1. It provides a reference framework against which emerging techniques are evaluated.
2. In factory settings, because capital costs must be minimized, hydroalcoholic extraction represents a realistic option, especially for bulk phenolic recovery from pomace.
3. Conventional protocols combine pretreatment and make it part of hybrid processes rather than obsolete stand-alone methods.

Recent publications prove that conventional extraction alone is increasingly considered insufficient when the objective is to maximize selectivity, decrease environmental impact, and improve process economics at scale [37,39,46].

5.2. Green and Intensified Extraction Techniques

Based on emerging technologies, ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), enzyme-assisted extraction (EAE), pressurized liquid extraction (PLE), and supercritical fluid extraction (SFE) are the most used for grapevine residues. UAE is important here because acoustic cavitation improves solvent penetration and disrupts cell structures, thereby increasing mass transfer while reducing the extraction time and solvent consumption. This method has been repeatedly reported as effective for recovering total phenolics, anthocyanins, and flavonoids from grape pomace and wine lees, especially when combined with ethanol–water systems or natural deep eutectic solvents [9,17,46,48]. MAE offers similar extraction advantages by rapidly heating the mixture. This detail enhances the release of bioactive compounds from different residue types. For canes and pruning wood, microwave-based protocols have shown notable promise for rapidly recovering stilbenes such as *trans*-resveratrol and ε-viniferin [6,8]. To situate these gains quantitatively, ultrasound-assisted extraction of grape canes has achieved total phenolic yields of 32.6 mg GAE/g DW at laboratory scale and 26.0 mg GAE/g DW after scale-up to a 1.5 L pilot volume (60 min, ethanol–water 50:50, v/v) [49], whereas exhaustive stilbene-targeted protocols spanning maceration, Soxhlet, fluidized bed, microwave-assisted, and accelerated solvent extraction have shown more than ten-fold differences in recoverable *trans*-resveratrol (from 0.49 to 6.03 mg/g DW) between the least and most effective conditions on the same cane substrate, confirming that technique choice, not only substrate composition, is a first-order determinant of reported yields [8].

EAE contributes a different mechanism, a hydrolysis-dependent pathway of cell wall polysaccharides through enzymes (pectinases, cellulases, and hemicellulases). This detail is

relevant for grape skins and pomace, where major phenolic compounds could be partially retained inside structural matrices that are strongly complexed. Recent studies indicate that enzymatic pretreatment can increase the recovery not only of free phenolics but also of compounds associated with the insoluble cell wall fraction, especially when EAE is combined sequentially with ultrasound or conventional solvent extraction [46]. PLE and SFE represent more technologically advanced solutions. PLE uses elevated temperature and pressure to improve solvent diffusivity and extraction kinetics, whereas SFE—most often based on supercritical carbon dioxide plus or without polar co-solvents—is especially suitable for non-polar or moderately polar fractions such as lipids and certain aroma-related compounds. These techniques offer significant advantages in selectivity and easy solvent recovery; however, their widespread industrial use is still constrained by capital cost, equipment complexity, and the need to control the process conditions for highly variable substrates [9,39,46]. A maintenance period after processing, until the extraction phase, is very relevant.

5.3. Deep Eutectic Solvents and Other Green Solvent Systems

One of the more notable recent shifts in grapevine waste valorization is the move toward deep eutectic solvents (DESs) and their natural counterparts (NADESs) in place of conventional organic solvents. These mixtures form when a hydrogen bond donor and acceptor are combined (choline chloride with organic acids, sugars or polyols), and their composition can be tuned to the substrate, so that a given phenolic class is solubilized more readily while toxicity and volatility stay low. On red grape pomace, NADESs coupled with ultrasound have given anthocyanin and total polyphenol recoveries comparable to conventional systems, with the added advantage that the extract can often be carried into a food or cosmetic formulation without exhaustive solvent removal [9,18]. Other reports point to improved bioaccessibility and functional performance, so far mostly at research scale and mainly in cases where the solvent is itself compatible with the final product matrix [9,46]. It is worth being explicit about the evidentiary status of these claims: the comparability of NADESs and conventional solvent recoveries is well established across multiple independent studies and can be treated as a reasonably mature finding, whereas the reported gains in bioaccessibility remain preliminary, resting on a smaller number of studies conducted at research scale, and should not yet be generalized to all NADESs–matrix combinations.

The enthusiasm for DESs and NADESs nevertheless deserves scrutiny. Viscosity is high enough to limit mass transfer, and because extractability depends on solvent composition, results are not always comparable between laboratories. Purification remains the awkward step: for isolated fractions intended for nutraceutical use, it is often the real bottleneck, much less so for extracts sold ready to use. The sustainability argument is sound, but solvent design still needs standardization, processes need to prove reproducible, and industrial acceptance has yet to follow; none of this has been backed so far by a convincing cost assessment. This is one reason why water, aqueous ethanol and subcritical water remain relevant options, with lower environmental burden, simpler scale-up and a regulatory path that smaller companies can realistically navigate [9,39,46]. Much of the work is still at laboratory scale, and translating it into high-volume production is the decisive step. Taken together, the yield ranges compiled in Table 3 indicate that pressurized liquid and enzyme-assisted protocols achieve the highest reported TPC values among the techniques compared here (up to ≈79 and ≈50 mg GAE/g DW, respectively, versus ≈47 mg GAE/g DW for conventional maceration), whereas ultrasound-assisted and DES-based methods remain broadly comparable to the conventional benchmark on this matrix; because these values originate from different pomace sources, solvent systems and Folin–

Ciocalteu calibrations, they should be read as indicative orders of magnitude rather than as a strictly matched ranking.

5.4. Purification, Fractionation, and Analytical Standardization

Extraction on its own rarely delivers a product standardized enough for industrial use, which is why filtration, centrifugation, membrane separation, liquid–liquid partitioning, resin adsorption and chromatographic fractionation now appear routinely in grapevine waste processing schemes. Such steps matter whenever the aim is to enrich a particular fraction, reduce the sugar content, remove non-phenolic solids, strip residual solvent, or deliver extracts reproducible against defined chemical markers. Stilbene-rich cane extracts, anthocyanin-enriched skin fractions and seed proanthocyanidin concentrates all depend on this kind of control, since composition determines nutraceutical functionality, shelf stability and market positioning [6,8,46]. Analytical standardization is equally important. Total phenolic figures alone are no longer adequate: chromatographic and spectrometric profiling, validated methods and consistent reporting units are what make studies comparable, and without them, the case for industrial valorization is weak [4,46,48].

5.5. Factors Affecting Extraction Efficiency and Selectivity

Extraction efficiency reflects the interaction between what the substrate is and how it is processed. On the matrix side, cultivar, growing region, climate, ripeness, the type of vinification (red or white) and post-harvest handling all shape how much of a target compound is present and how easily it can be released. Moisture content matters a great deal, since fresh and dried pomace differ both in solvent penetration and in oxidative stability. Lignification plays a comparable role for canes (stilbenes) and pruning wood, where it governs accessibility. On the process side, the variables are numerous: particle size, solvent, pH, solid-to-liquid ratio, time, temperature, ultrasonic power, microwave intensity, enzyme use, and whatever pretreatment preceded them. Optimization is not simply a matter of maximizing yield; the aim is to keep the target compounds intact and obtain an extract fit for its intended application [6–9,46,48].

5.6. Industrial Relevance, Scale-Up, and Process Integration

Direct techno-economic and life cycle comparisons between extraction techniques remain scarce for grapevine waste specifically, but the limited evidence available indicates that process choice carries substantial cost and environmental consequences. A combined techno-economic assessment (TEA) and life cycle assessment (LCA) of polyphenol recovery from red wine pomace found that pressurized liquid extraction (PLE) with an ethanol–water mixture containing CO_2 as co-solvent delivered markedly higher polyphenol output than conventional acetone–water solvent extraction (572 versus 340 tons GAE per year, i.e., approximately 79 versus 47 mg GAE/g DW, for a plant processing 20,000 t of wet pomace per year), but required substantially higher capital expenditure and performed worse in the life cycle assessment, mainly because of its higher solvent-to-dry-matter ratio, illustrating that the technique with the highest yield is not automatically the most favorable one, environmentally or economically [50]. A separate life cycle comparison spanning subcritical water extraction, ultrasound-assisted extraction, conventional solvent extraction, and microwave-assisted extraction of wine residues found that no single method was universally best: microwave extraction from exhausted grape marc had the highest environmental impact overall, driven by low yields combined with high energy use during freeze-drying, whereas subcritical water extraction from red grape stalks was the most sustainable option, benefiting from high efficiency, the use of water as solvent, and the naturally higher polyphenol content of red variety residues; across all methods, drying was consistently the dominant contributor to greenhouse gas emissions, and, in a sensitivity

analysis of the subcritical water scenarios, replacing fossil-based energy with renewable sources reduced the overall impact by approximately 90% [51]. These findings indicate that the environmental and economic performance of an extraction route depends jointly on the technique, the specific residue fraction processed, and the energy source used for drying and solvent recovery, rather than on the extraction principle alone.

Industrially, the best method is not necessarily the one with the highest laboratory yield. What counts is the balance between recovery, solvent safety, throughput, cost, reproducibility and fit with downstream product development, which makes process selection a techno-economic decision rather than a purely chemical one. UAE and well-optimized hydroalcoholic extraction are the most plausible near-term candidates, since the equipment is accessible and polyphenol recovery is good. MAE, PLE, SFE and DES-based routes make more sense for higher-value products, where added selectivity or differentiation justifies the extra complexity. Hybrid schemes are also described in the literature: one fraction is extracted for bioactives while the residual biomass goes to fiber ingredients, adsorbents, bio-based materials or energy recovery. Approaches of this kind fit circular bioeconomy objectives most closely and are likely to set the direction of both research and industrial practice [2,4,6,9,39,44,46]. Several of the extraction technologies reviewed in this section reappear directly in Section 2 not as an alternative to fermentation but as its partner: enzyme-assisted extraction shares its underlying hydrolytic mechanism with solid-state fermentation, and hybrid extraction–fermentation cascades, discussed in detail in Section 2.6, depend on the purification and standardization steps introduced here being compatible with a subsequent microbial step rather than treated as a terminal process.

Table 3. Summary of major extraction methods applied to grapevine waste valorization, with representative yields expressed on a dry weight (DW) basis (substrate in parentheses).

Method	Principle/Process Feature	Main Advantages	Main Limitations	Typical Target Compounds/Fractions; Representative Yields (DW)	Industrial Relevance	References
Conventional solid–liquid extraction/maceration	Diffusion-based extraction using aqueous ethanol, methanol, acetone, or hydroalcoholic mixtures	Simple, low capital cost, easy to reproduce, useful as reference method	Long extraction time, high solvent consumption, limited selectivity, possible thermal degradation	Total phenolics, anthocyanins, flavonoids, tannins, stilbenes; TPC ≈ 47 mg GAE/g DW (acetone–water, red pomace); *trans*-resveratrol 0.49–4.19 mg/g DW (maceration, cane)	Still relevant for bulk extraction and hybrid industrial processes	[8,9,39,46,50]
Soxhlet extraction	Continuous hot solvent recirculation through dried solid matrix	Exhaustive extraction, standardized laboratory method, good for comparative studies	High temperature exposure, long duration, solvent-intensive, limited industrial suitability	Phenolics from dried pomace, seeds, and canes; *trans*-resveratrol 5.17 mg/g DW in the first methanol step (cane)	Primarily analytical and method development relevance	[8,46]
Ultrasound-assisted extraction (UAE)	Acoustic cavitation enhances solvent penetration and mass transfer	Shorter extraction time, lower solvent use, good phenolic recovery, mild conditions	Scale-up may require careful control of energy distribution and matrix heterogeneity	Polyphenols, anthocyanins, flavonoids, wine lees extracts; TPC 10.6–32.6 mg GAE/g DW (cane, laboratory and 1.5 L pilot scale)	High near-term industrial potential for food and cosmetic ingredients	[9,16,17,46,49]

Table 3. *Cont.*

Method	Principle/Process Feature	Main Advantages	Main Limitations	Typical Target Compounds/Fractions; Representative Yields (DW)	Industrial Relevance	References
Microwave-assisted extraction (MAE)	Rapid internal heating of the solvent–matrix system	Fast processing, improved release of bound compounds, useful for stilbenes and phenolics	Risk of localized overheating, equipment cost, optimization required for different matrices	Stilbenes from canes, phenolics from skins, pomace, and seeds; *trans*-resveratrol 0.77–0.81 and ε-viniferin 1.36–1.40 mg/g DW (pruning wood)	Promising for high-value extracts, moderate scale-up maturity	[6,8,46]
Enzyme-assisted extraction (EAE)	Enzymatic hydrolysis of cell wall polysaccharides to release entrapped compounds	Improved recovery from complex matrices, mild conditions, suitable as pretreatment	Enzyme cost, longer pretreatment, sensitivity to pH and temperature	Cell wall-associated phenolics, pomace and skin fractions; TPC 38.5 mg GAE/g DW (tannase–cellulase, pisco pomace)	Useful in combined and cascade processes rather than as a stand-alone method	[46,47]
Pressurized liquid extraction (PLE)	Elevated temperature and pressure improve solvent diffusivity and extraction kinetics	Reduced extraction time, high efficiency, improved process control	Equipment complexity, capital cost, possible degradation of sensitive compounds	Phenolics, flavonoids, selected polar and semi-polar compounds; TPC 50.0 mg GAE/g DW (pisco pomace) and ≈ 79 mg GAE/g DW (ethanol–water–CO_2, red pomace); *trans*-resveratrol 6.03 mg/g DW (accelerated solvent extraction, cane)	Suitable for more advanced industrial platforms and standardized production lines	[8,46,47,50]
Supercritical fluid extraction (SFE)	Use of supercritical CO_2, optionally with co-solvents, for selective extraction	Low solvent residues, good selectivity, strong sustainability profile for suitable fractions	High capital cost, lower efficiency for highly polar compounds without modifiers	Seed oils, aroma-related fractions, moderately non-polar compounds; seed oil yield 5.9–13.6% (*w*/*w* of seed, eight cultivars)	Best suited to premium applications where purity and solvent recovery are priorities	[46,52]
DES-/NADES-based extraction	Tailored deep eutectic solvents improve solubilization of target phenolic classes	Reduced volatility, potential formulation compatibility, strong green chemistry appeal	High viscosity, variable analytical comparability, downstream purification challenges	Anthocyanins, total polyphenols, tailored phenolic fractions from pomace and skins; TPC 43.0 mg/g DW (choline chloride–oxalic acid DES, red pomace)	Promising for specialized food, cosmetic, and functional ingredient applications	[9,18,46]

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