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Review

# Technological Aspects and Potential Cutaneous Application of Wine Industry By-Products

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**Abstract:** The biomass of vinification results in up to 20% by-products (seeds, skins, pulp, and/or stems) that can be used in the production of diverse functional food, nutraceutical, pharmaceutical, and cosmetic ingredients, mainly due to their high polyphenol content. Conventional polyphenol extraction techniques are based on the use of solvents that are harmful to health and to the environment, creating a demand for sustainable complementary initiatives that mitigate part of the environmental effects and offer consumer safety. Current advances in these technologies allow for the recovery of valuable antioxidants from winemaking by-products free of hazardous solvents, biocompatible, and in compliance with international sustainable development guidelines. Nanotechnology has gained prominence in the development of green technologies to reduce or eliminate toxic agents and improve the stability and bioavailability of waste polyphenols. These efforts have led to the application of bioactive compounds from wine by-products in the development of more efficacious sunscreens, as a skin protection approach, and improvements in the antioxidant effectiveness of nanocarriers with potential use in the promotion of cutaneous health. We aimed to present different extraction and encapsulation technologies for biologically active compounds from wine by-products (*Vitis vinifera* L.). We also focused on a particular application of such compounds towards the development of value-added skin protection products aligned with a sustainable circular economy.

**Keywords:** *Vitis vinifera* L.; winemaking; by-products; circular economy; green extraction; health; biotechnology; nanotechnology



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## 1. Introduction

In 2022, wine production volume was estimated at between 257 and 262 million hectoliters (mhL), and the top four producer countries were Italy (50.3 mhL), France (44.2 mhL), Spain (33.0 mhL), and the United States (EUA) (23.1 mhL) [1]. According to Tacchini et al. [2], each liter of wine produces around 166 g of grape pomace. Wine by-products contain a wide variety of compounds, such as nitrogen, salts, fats, and the main ingredients of economic interest, "natural antioxidants", notably phenolic compounds, representing up to 20% of all wine biomasses (seeds > skin > pulp) [3–9].

Winemaking is an important market in the food industry. About 30% of vinified grapes represent nearly 20 million tons of by-products [10], which can be reused for different purposes, such as in agriculture, livestock, distillery, biorefinery, and as a potential source of phytochemicals for health [10,11]. However, when wine by-products are discarded without proper treatment, they can cause environmental concerns for the water system, animal and insect infestations, and soil acidification [5,7,8,12]. Although the European Commission Decision 2000/532/EC includes waste from agriculture and horticulture, by-products from wine and beer production remained excluded, unlike spirit distillation residues [4,13].

About 70% of grapes' phenolic content remains in the organic residue (Table 1) [6,14]. The chemical composition and bioactivities of wine residues can be influenced by edaphoclimatic conditions and winemaking technology, including similar varieties grown at other sites [7,11,15]. Grapes are rich in health-promoting polyphenols [3,5] and *Vitis vinifera* L. is one of the most used polyphenol-rich grape species cultivated worldwide to produce wine, surpassing 70 million tons [5,16–18].

**Table 1.** Main compound classes of red and white grape pomaces from winemaking.

| By-Product | Compounds | | References |
|---|---|---|---|
| | Red Grape | White Grape | |
| Grape pomace (mixture) | Phenolic acids; flavonoids; proanthocyanidins; anthocyanins; stilbenes; protein; lipid; fiber; and ash | Phenolic acids; flavonoids; proanthocyanidins; stilbenes; polysaccharides | [7,11,19–21] |
| **Grape seeds** | Phenolic acids; flavonoids; proanthocyanidins; anthocyanins lignocellulosic material, oil (linoleic—ω6 > oleic—ω9 acid); proteins; sugars; minerals; polysaccharides (cell wall) | Phenolic acids; flavonoids; proanthocyanidins; stilbenes | [7,20,22–24] |
| Grape skins | Phenolic acids; flavonoids; anthocyanins; polysaccharides | Phenolic acids; flavonoids; proanthocyanidins; stilbenes | [7,20,22] |
| Stalks | Phenolic acids; flavonoids; proanthocyanidins; anthocyanins; polysaccharides; ash; cellulose; proteins; tannins; lignin; hemicelluloses; monosaccharides | Phenolic acids; flavonoids; proanthocyanidins | [23,25,26] |

The synergy of the circular economy involves reducing wine grape pomace and increasing the useful life of bioresources [7,27] as functional food, nutraceutical, pharmaceutical, and cosmetic ingredients [5,7,28], which contributes positively to the environment, society, and the economy itself, as recommended by the United Nations Sustainable Development Goals [27]. Winery biowaste management strategies (first and second generation) are requirements for the development of a sustainable bioeconomy [16,29]. First-generation biowaste is sent to facilities for composting, landfill, or biogas via anaerobic digestion; second-generation biowaste is directed to green technology, valuing products such as seed oil, fibers, tartaric acid, squalene, and ethanol, for example [2,29]. It should also be taken into consideration that in many European and non-European countries, more than 5% of organic waste is prohibited in landfills. Winemaking residues with lower investment and transportation costs may be recycled if cooperatives in strategic locations assist the wineries. In Bulgaria, for example, waste-free technology was introduced to process winemaking by-products [8]. In this review, we aimed to present different extraction and encapsulation technologies of biologically active compounds from wine by-products (*Vitis vinifera* L.). We also focused on a particular application of such compounds towards the development of value-added skin protection products aligned with a sustainable circular economy. From our perspective, we believe this review could encourage the following: sustainable development of a circular economy based on wine agroindustry (zero waste and reduction in environmental damage and damage to living beings); the recovery of active compounds from winemaking residues to obtain products with high added value for health, especially for skin protection; increasing the visibility of functional polyphenols from *V. vinifera* by-products; and the safe and effective application and consumption of skin protection products based on wine residues.

## 2. Opportunity to Obtain Value-Added Products in Circular Economy

The evident climate changes outline a worrying panorama in several sectors. It is estimated that around 1/3 of agricultural products are wasted before reaching the market, leading to environmental pressure. Although considered comparatively more polluting, regarding greenhouse gases, livestock shows reduced loss and waste. The "healthy" food system is represented by, for example, the production of vegetable proteins, using up-to-date agricultural techniques, restricting the pollution of terrestrial and aquatic ecosystems, limiting, or replacing fertilizers, such as nitrogen and phosphorus, and the recycling of water resources. This complex scenario requires complementary initiatives that mitigate part of the environmental effects arising from the agricultural sector and its influence on food and nutrition security [30]. In this context, the education of the population is urgent since once people become aware of the problem of natural adversities, they can actively participate in reducing the pressure on the environment.

Food choices (type, quantity, etc.) associated with maintaining people's health and/or reducing the incidence of non-communicable diseases can help achieve environmental sustainability goals by curbing environmental degradation [31]. Viticulture generates various residues from pruning the vine and the fruits used in winemaking (stems, pomace, and grape seed), being a small part of these residues that is reused in value-added products. Existing technologies and the demand for by-products can help to reallocate such wastes [32]. The stalks and stems of pruning vines are considered sources of procyanidins, lignin, cellulose, and hemicellulose. The cellular contents of these wall components depend on the cultivar, winemaking, and destemming processes. The stalks, for example, represent an average of 25% weight of the grape pomace [33]. Additionally, the effluent can be used for other purposes, for example, as a medium for microalgae cultivation [34]. Researchers suggest a sequence of zero-waste alternatives applying circular economy guidelines as follows: (I) the recuperation of higher value compounds, such as polyphenols through "green" techniques (biorefinery of economically viable and environmentally correct agro-industrial residues); (II) anaerobic biodegradation for biogas production; and (III) composting of depleted biomass [35] (Figure 1). Obtaining biogas using processed water, initiated during the hydrothermal carbonization of depleted grape pomace, can enable the preservation of energy and physical–chemical properties of hydro charcoal, suggesting its use in adsorbing atmospheric and water pollutants.

Polyphenols from wine production residue are natural raw materials that can help to prevent diseases [36]. Studies indicated their beneficial effects, mainly linked to the elimination and transmission of reactive oxygen species through the processes of autoxidation by donating hydrogen atoms or electrons and the synthesis of antioxidant molecules involved in the signaling of enzyme-linked receptors [17,36]. An overview of recent trials (Table 2) reports a strong antioxidant effect of white and red wine grape pomace extracts mostly performed using in vitro assays [5,11,20,24,25,28,37–48]. The bioaccessibility and bioavailability potential of phytochemicals of white wine grape pomace (*V. vinifera* cv. Zalema grapes) depend on the type of by-product, digestion phase, and recovery of phenolic groups. The phenolic compounds in seeds and pomace extract significantly decreased after gastric digestion compared to undigested samples. The total contents of phenolic acids (skin extract) and flavanols (stem and pomace extracts) increased significantly after gastric and intestinal digestion compared to undigested samples. The antioxidant activity of seed and stem extracts increased (~149% and 219%, respectively) after intestinal digestion. However, it decreased in skin and pomace (~52% and 75%, respectively) [25]. Muscat grape pomace drying revealed the negative impact of time and temperature (6 h at 80 °C) on flavanol and monomeric anthocyanins content and radical scavenging potential compared to the untreated (fresh) material. Catechin was the most thermolabile among several compounds isolated from those raw materials, and it was followed by rutin. The researchers pointed out that the recovery of polyphenols should be carried out using low-impact extraction [37]. Even though many investigations indicate the abundance of polyphenols and the high antioxidant potential of the fermented residues from wine production after simulated gastrointestinal digestion, further studies are needed for exploring their applicability in human health and well-being.

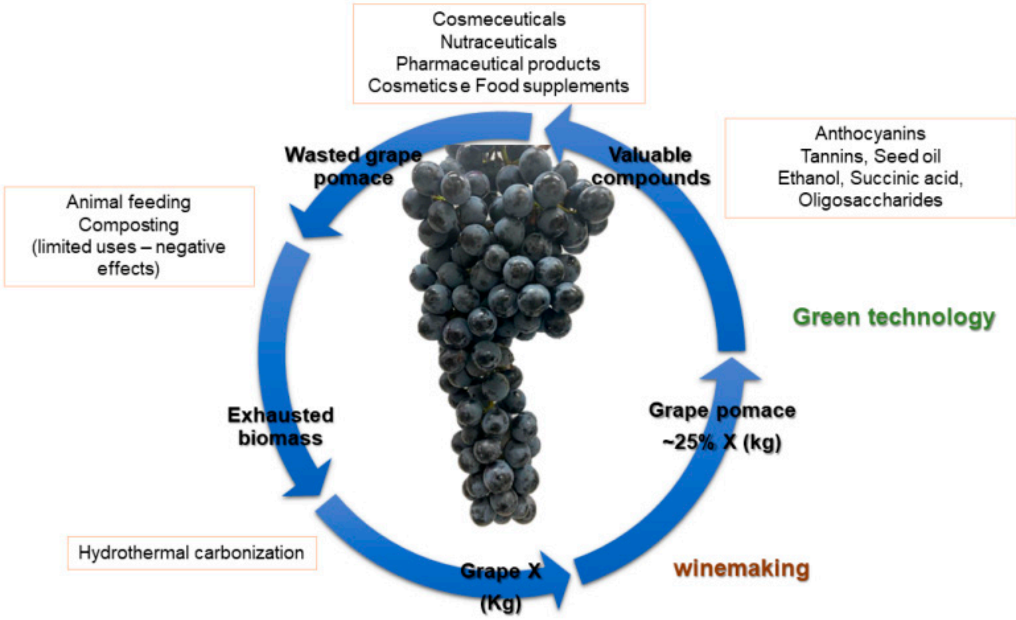


**Figure 1.** Simplified outline of the circular economy application for the valorization of winemaking by-products.

Bioactives from winemaking residues have attracted attention due to their health benefits and potential economic and social improvements for the cosmetic and pharmaceutical industries [49]. An example is tocopherol, which can act as an antioxidant, anti-inflammatory, hepatoprotective, cardioprotective, and anticancer agent. Grape pomace pre- and post-fermentation from red and white wines demonstrated considerable concentrations of tocopherol. The red grapes were slightly richer in tocopherols than the white ones, and the alcoholic distillation of the waste mixture moderately reduced the tocopherol concentration, even so, resulting in a valuable secondary ethanolic extract for health applications [6].

The efficient industrial extraction of waste phytochemicals provides greater extractive yield, reduction in discard, and economic gains with high-value substances, such as alcohol, tartaric salts, food pigments, and grape seed oil. Tempranillo grape has been shown to contain higher phenolic content and antioxidant activities in red grape seeds and similar values in washed grape pomace [7]. The main compounds found in hydroethanolic grape pomace extracts were flavonoids and proanthocyanidins, which corroborated the antioxidant capacity of such material [50]. Although many papers proved the significant content of antioxidants, mainly polyphenols, the number of studies in the cosmetic and pharmaceutical areas that attest to these benefits in humans is still insufficient to stimulate the large-scale production of phenolic derivatives from winemaking in promoting health.

Highly bisphenol-stable aqueous grape pomace extracts were obtained using microwave hydro-diffusion and gravity (MHG) of Sicilian grapes, including Syrah, Perricone, and N. d'Avola. In the aqueous extract, high levels of enocyanin were found. Gallic acid and its ethyl ester derivative reached considerable amounts in the Perricone grape, followed by hydroxybenzoic and syringic acids. Quercetin was predominant in the Perricone and Syrah aqueous extracts, and resveratrol was abundant in the Perricone pomace [51].

**Table 2.** Biological effects associated with bioactive compounds from winemaking by-products (red/white *V. vinifera*).

| By-Product | Cultivar | Chemical Compounds | Bioactivity | References |
| --- | --- | --- | --- | --- |
| Whole grape pomace and/or skins/seeds/stems separated | C. Sauvignon | Total phenolics and flavonoids, flavonoids (dihydroflavonol and flavonols), anthocyanins, and procyanidin dimers and trimers | Efficacy and safety photoprotective in volunteers and in vitro antioxidant activity model | [28,41] |
| | Mixture of Sangiovese and Montepulciano | Total polyphenols, flavonoids, tannins, and anthocyanins | In vitro antioxidant and anticholesterolemic (7a-hydroxylase—7a1 and sterol 27-hydroxylase—cyp27a1) activities | [39] |
| | Zalema | Total phenolic, phenolic acids, flavonoids (flavanols and flavonols), and dimeric proanthocyanidins | In vitro antioxidant and antiproliferative activities on the human colon adenocarcinoma cells (Caco-2) | [25,48] |
| Seed + skins and/or skins/seeds separated | Pinot Noir and Merlot | Ash, protein, and fat content, soluble sugar, insoluble and soluble dietary fiber, pectin, total phenolic, anthocyanin, flavonoid (flavanol), and condensed tannin | In vitro antibacterial (*Escherichia coli* and *Listeria innocua*) activity | [47] |
| | Not mentioned, only (*V. vinifera*) | Phenol acids, flavan-3-ols, flavonols, and anthocyanins | In vitro antioxidant, cytotoxic (human cervical carcinoma—HeLa and human breast adenocarcinoma—MCF-7), and antibacterial (*Klebsiella pneumoniae*, *Klebsiella pneumoniae* ESBL, and *Morganella morganii*) activities | [20] |
| | Nero d'Avola | Polyunsaturated fatty acids, polyphenols, proanthocyanidins, flavonoids, anthocyanin total, and stilbenes (resveratrol) | In vitro antioxidant (human skin fibroblast HS-68) and antiproliferative hepatoma Hep-G2) effects | [24] |
| | Grenache, Syrah, Carignan, Mourvedre, Counoise and Alicante | Total phenols, anthocyanins, and proanthocyanidins | In vitro antihypertensive potential in a chronic disease model | [42] |

**Table 2.** *Cont.*

| By-Product | Cultivar | Chemical Compounds | Bioactivity | References |
| --- | --- | --- | --- | --- |
| Skins | Tempranillo, Tintilla de Rota, C. sauvignon, Petit verdot and Syrah | Hydroxybenzoic and hydroxycinnamic acids, flavan-3-ols, tyrosol, flavonols and anthocyanins | In vitro antioxidant activity | [38] |
| | Barbera, Croatina, Dolcetto, Grignolino, Nebbiolo and Pinot Nero | Total phenolics, flavonoids (flavonols) anthocyanins, and proanthocyanidin | In vitro antioxidant and anti-glycation activities | [40] |
| Not specified, only "grape pomace" | Carignano | Organic acids, phenolic acids, flavonoids, stilbenes, anthocyanins, proanthocyanidin, triterpenes, lipids | In vitro model for the prevention of oxidative stress-induced ROS (3T3 cells) | [45] |
| | Merlot | Flavonoids (flavan-3-ols, galloyl derivatives, and flavonols), anthocyanins and procyanidin B-type (epi)catechin dimer/trimer/tetramer | In vitro antioxidant, cytotoxic, and antibacterial activities | [5] |
| | Muscat | Phenolic acids, flavonoids (Catechin, rutin, and quercetin), and anthocyanins | In vitro free radical scavenging activity | [37] |
| | Nasco | Hydroxybenzoic acids (gallic acid), (+)-catechin, (-)-epicatechin, condensed tannins | In vivo neuroprotective effects | [44] |
| | Mixture of Trebbiano and Verdicchio | Phenol acids, flavanols, tannins, and mono-glycoside stilbenes | In vitro antioxidant, anti-tyrosinase, and anti-inflammatory on human embryonic kidney cells (HEK293) activities | [11] |
| | Chenin Blanc, Petit Verdot, and Syrah | Hydroxybenzoic acid (gallic acid), flavan-3-ols and flavonols, anthocyanins, and condensed tannins | In vitro antioxidant and anti-inflammatory (Tumor necrosis factor-alpha—TNF-α) activities | [43] |
| Extract and process patent protected | Albariño | Non-flavonoids, flavonoids, proanthocyanidins B, and total procyanidins | In vitro antimicrobial and anti-parasitic activities | [46] |

The relevant enzymes of unconventional habitats, such as wild oenological industry yeasts (*S. cerevisiae*) isolated from two different white grape pomace (Prosecco and Moscato), have shown to be interesting for future biotechnological applications [52]. A review evaluated that treatment combined with cellulase and pectinase enzymes increased the extraction of phenolic compounds from wastes, and it also could overcome the cost and security limitations of the current technologies [4]. Ethanol and aqueous extracts of dried white grape pomace obtained using enzyme-assisted extraction (EAE) showed antioxidant, anti-tyrosinase, and anti-inflammatory properties [11].

Nowadays, consumers are interested in minimally processed products and the use of natural antioxidants for food preservation. Considering the high content of antioxidant "polyphenols" remaining in wine grape pomace, hamburgers were mixed with 0, 2, and 4% of pomace. In these conditions, the pH, cooking yield, and patty colors decreased, while the shear strength and hardness of Allo–Kramer increased as pomace was added. Burgers containing by-products did not differ in flavor, juiciness, and hue compared to control burgers [53].

The spontaneous microbiological deterioration of grape pomace extracts led to significant losses in polyphenols and, consequently, antioxidant activity. To minimize these effects, methods of stabilization of phytochemicals from grape pomace were also employed, such as drying methods, vacuum drying oven, and lyophilization [54]. Researchers using high voltage atmospheric cold plasma—HVACP (60 kV)—in different periods (5, 10, and 15 min) to modify the surface properties of wine by-products and enhance the recovery of active compounds found that HVACP-treated grape pomace was able to increase up to 22.8% of the total phenolics and 34.7% of the antioxidant effect. The use of this innovative technology enabled the increase in the content and nutritional quality of functional foods and nutraceuticals based on the by-product of winemaking [55]. Grape pomace flours are also a source of nutrients and bioactive compounds. However, there are risks to human health that may come from the soil or external contamination, like heavy metals. European Commission regulations recommend in-depth studies, logistical and handling controls of wine waste before insertion into industrial food production [56].

## 3. Valorization of Winemaking Residues—Use of Technologies

According to different authors [9,57], the replacement of conventional technologies (solid-liquid extraction, heating, grinding) with unconventional ones—pulsed electric field extraction (PEFE), high voltage electrical discharge, pulsed ohmic heating, ultrasound-assisted extraction (UAE), EAE, microwave-assisted extraction (MAE), sub- and super-critical fluid extraction (SFE $CO_2$), and pressurized liquid extraction—for the recovery of valuable antioxidants in winemaking by-products presents indisputably greater efficiency and selectively extractive power and consonance with "green" extraction methods. Such technologies are promising, and the challenges of equipment, installation costs, and waste processing on a pilot scale must be overcome before industrialization. Table 3 shows studies on conventional and non-conventional techniques that have been used to improve the extraction, separation, and purification of chemical constituents from wine by-products (*V. vinifera*) with potential applications in cosmetics, pharmaceuticals, nutraceuticals, and food supplements.

**Table 3.** Techniques used to extract, separate, and purify chemical constituents from winery by-products (*V. vinifera* grape).

| Cultivar | By-Product | Technique | Compound | References |
|---|---|---|---|---|
| Red Saperavi and white Rkatsiteli grapes | Skins and seeds | GD, SLE | Tocopherols | [6] |
| Red Chardonnay grape | Seeds, grape skin, and stems | SLE, HT, MAE | Polyphenols (gallic acid) | [50] |

**Table 3.** *Cont.*

| Cultivar | By-Product | Technique | Compound | References |
|---|---|---|---|---|
| Red Tempranillo grape | Red grape pomace, seeds, and seed flour | GD, CCD, HT, SLE | Total protein, lipid, fiber, ash, polyphenols | [7] |
| Red Prokupac grape | Skin, seed, stem, and whole pomace | GD, SLE, ST, FT, | Polyphenols | [15] |
| White Albarino grape | Seeds | MSPD | Polyphenols | [16] |
| Red Alicante Bouschet grape | Skins | MR-XAD-7HP | Polyphenols (anthocyanins) | [58] |
| Red Syrah, Perricone and N. d'Avola grapes | Skins, seeds, residual pulp, and stems | MHG | Polyphenols | [51] |
| Red Merlot grape | Grape pomace | EAE | Polyphenols | [5] |
| Red wine grape | Grape pomace (whole and seedless) and seeds separated | EAE | Polyphenols | [59] |
| White Trebbiano and Verdicchio grapes | Grape pomace | EAE | Polyphenols | [11] |
| Red Sangiovese and Montepulciano grapes | Skins, seeds, petioles, and stalks | EAE | Polyphenols | [39] |
| Red Sagrantino grape | Skins and seeds | GD, MacE | Polyphenols | [3] |
| Red Tempranillo grape | Grape pomace | GD, SE, SoxE, CT, DNF | Polyphenols | [9] |
| Red grape | Grape pomace powder | GD | Polyphenols | [18] |
| Red Syrah, Merlot, and C. Sauvignon grapes | Grape pomace (seedless) and seeds | SLE | Polyphenols | [53] |
| White Auxerrois and P. Blanc grapes Red Gamay and P. Noir grapes | Skins, seeds, and residual stalks | GD, SLE, UAE | Polyphenols | [54] |
| Not mentioned | Grape pomace | GD, SLE, ST, HT, CT, FT | Polyphenols | [60] |
| Red C. Sauvignon grape | Grape pomace (stemless) | GD, HVACP | Polyphenols | [55] |
| Red Merlot grape | Grape pomace | GD, SLE, RA, | Carbohydrates and polyphenols | [61] |
| Red Tempranillo grape | Grape pomace | GD, PHWE- NADES | Polyphenols (anthocyanins) | [62] |
| Red Tannat grape | Skin powder | GD, SLE, MacE, UAE, FT | Carbohydrates, protein, monomeric anthocyanins, polyphenols | [63] |
| Red Merlot and Syrah grapes | Grape pomace | GD, SLE, UAE, SFE $CO_2$ + CS | Polyphenols | [64] |
| Red Muscat of Hamburg grapes | Grape pomace | HT, ST, US-NADES | Polyphenols | [65] |
| Red Graciano grapes | Grape pomace | GD, SLE, ST, CT | Polyphenols | [66] |
| Red P. Noir grape | Grape pomace seedless | GD, SLE, HT, ST, FT | Cellulose | [67] |
| Red grape | Seeds and stalks | GD, SLE, ST, CT | Polyphenols | [23] |
| Red Cannonau red grape | Grape pomace | SLE, ST, CT, pellets re-dispersed in olive oil, ST, CT | Polyphenols | [68] |

**Table 3.** *Cont.*

| Cultivar | By-Product | Technique | Compound | References |
|---|---|---|---|---|
| Red Merlot grape | Seeds | GD, SLE, CT | Polyphenols (catechins) | [36] |
| Red Cannonau grape | Grape Pomace | SLE, MacE, CT, | Polyphenols | [69] |
| Non mentioned | Grape pomace | GD, SLE, HT, FT | Polyphenols (tannins) | [70] |

Conventional Technologies: centrifuged (CT), filtering (FT), grinding (GD), heating (HT), Maceration Extraction (MacE), solid–liquid extraction (SLE), Soxhlet Extraction (SoxE), stirring (ST). Non-Conventional Technologies: Centrifugal Force (CF), Counter-Current Diffusion (CCD), Diananofiltration (DNF), Enzyme-Assisted Extractions (EAE), High Voltage Atmospheric Cold Plasma (HVACP), Matrix Solid-Phase Dispersion (MSPD), Microwave-Assisted Extraction (MAE), Microwave Hydrodiffusion and Gravity (MHG), Pressurized Hot Water Extraction and Natural Deep Eutectic Solvents (PHWE- NADES), Resin Adsorption (RA) Supercritical Fluid Extraction-$CO_2$ co-solvent (SFE $CO_2$ + CS), Ultrasonic-Assisted Deep Natural Eutectic Solvent Extraction (US-NADES), Ultrasound-Assisted Extraction (UAE), and XAD-7HP Macroporous Resin (MR-XAD-7HP).

The critical points of bioactive extraction from agro-industrial residues for use in food include the choice of biodegradability and non-toxicity of solvents and the physical–chemical conditions. Combined extractive methods can improve the separation and purification of phenolic compounds from grape pomace. Solid–liquid extraction with hydroethanolic solution and fractionation through membrane filtration according to their molecular weight, with less energy consumption and at low temperatures, increasing the recovery of phenolics. However, due to the similarity of molecular weight of the phenols and carbohydrates, it was not possible to separate them by such a process, but they were successfully separated through a process of adsorption on resin and vacuum evaporation. This technique separates the phenols according to the dipole–induced dipole interaction [61]. MSPD is an emerging technique used for the extraction of phytochemical or organic contaminants from food, employing low amounts of samples, sorbents, and solvents [71]. Also, it is considered an efficient method to extract antioxidants with neuroprotective activity from viticultural residues [16].

To attain an increased yield of anthocyanins from grape pomace after vinification applying sustainable strategies, the implementation of pressurized hot water extraction (PHWE) combined with NADES satisfactorily met the extraction efficiency of the reddish pigments [62]. Recently, the literature pointed out the technological potential of NADES solvents as a promising green alternative characteristic of biodegradability and better extraction efficiency for polyphenols extraction from grape pomace [72,73]. NADES achieved extractive yields like those obtained with organic solvents and, in an optimized process, doubled them [73]. The acidified hydroalcoholic solution of grape skin pomace combined with a mixture of organic solvents was more effective in extracting polyphenols than other tested techniques [63]. The development of technologies aimed at removing seeds from fresh wine waste directly in the winery makes it possible to minimize the disposal of organic residue [49] and increase the source of income, mainly for small winegrowers with environmental responsibility.

## 4. Delivery Systems Based on Bioactive from Wine By-Products

Advances in nanotechnology have led to the development of innovative and safer nanoparticles that do not use toxic chemicals in their synthesis, further supporting the development of the bioeconomy based on winemaking residues. Table 4 exhibits a compilation of studies on the application of technologies with phenolic metabolites recovered from winemaking, showing that these systems can contribute to the antioxidant efficacy of promising products applied in the prevention of various health problems [23,36,65–70,74].

**Table 4.** Carrier systems of/for bioactive(s) of the grape pomace (V. vinifera) from vinification for health promotion.

| Carriers | Winery Waste | Encapsulation or Nanoparticle | Mean Diameter (nm) | Recovery or Encapsulation Efficiency (%) | Compound (s) | Application (s) | References |
|---|---|---|---|---|---|---|---|
| Liposomes | Grape pomace cv. Graciano extract | An aqueous dispersion containing extract and phospholipid lipoid® S75 was sonicated | 104 | 75 ± 30 | Phenol acids, flavonoids, mainly anthocyanins | Treatment of oxidative skin conditions | [66] |
| Liposomes | Grape seeds cv. Merlot extract | Lipoid® S100, lipid, vitamin E, and Tween® 80 were dissolved in ethanol after aqueous dispersion containing extract and polysorbate 80 was added; followed by agitation, evaporation, and membrane filtration | 179.8–420.2 | - | Flavonoid (catechin) | Sustainable packaging and antioxidants for food products | [36] |
| Microemulsions | Grape pomace cv. Muscat of Hamburg extract | Isopropyl-myristate, Span® 20, and Tween® 80 were mixed, the extract was added, and after stirring | - | - | Hydroxycinnamic acid (caftaric acid) and flavonoids (rutin, quercetin, catechin) | Natural chemical stabilizer and the antioxidant of nutraceuticals and cosmetics | [65] |
| Nanocrystals | Grape pomace seedless cv. P. Noir extract | The cellulose isolated was hydrolyzed with sulfuric acid. The recovered material was washed with water until forming a colloidal suspension that was dialyzed until neutral pH | 7–8 | 80.1 | Polysaccharides (cellulose) | Non-toxic reinforcing materials for packaging or gels in food and pharmaceutical products | [67] |

**Table 4.** *Cont.*

| Carriers | Winery Waste | Encapsulation or Nanoparticle | Mean Diameter (nm) | Recovery or Encapsulation Efficiency (%) | Compound (s) | Application (s) | References |
|---|---|---|---|---|---|---|---|
| Nanoparticles | Grape pomace extract | Aqueous extract of grape pomace rich in tannins and the silver nitrate solution were mixed (1:10, respectively) in a magnetic stirrer, after concentrated and water was added to the separated pellet | 15–20 | - | Condensed tannins | Development of antidiabetic, antioxidant, and antimicrobial products | [70] |
| Phospholipid vesicles | Grape pomace cv. Cannonau extract | Dispersions containing Lipoid® S75 (120 mg), pellet extractive olive oil (100 mg), and, 1 mL of grape pomace extract in a mixed solvent system were sonicated | 150–193 | 98 and 84 | Hydroxybenzoic acids, flavan 3-ols, flavonols, anthocyanins, fatty acids | Antioxidants for pharmaceutical and/or cosmetic products | [68] |
| Phospholipid vesicles | Grape seeds and stalks extracts | Lipoid® S75, Tween® 80, and water or sodium hyaluronate | 62–139 | 90–96 | Phenol acids and flavonoids | Treatment of oxidative skin disorders | [23] |
| Phospholipid vesicles | Grape pomace cv. Cannonau extract | Aqueous dispersion containing Lecinova®, extract, water, gelatin or Nutriose® FM06, or both were sonicated | 128–175 | 65–88 | Hydroxycinnamic and hydroxybenzoic acids, flavanols, flavonols anthocyanins | Gastrointestinal protection | [69] |

The encapsulation technology of active compounds with polymeric materials on a micrometer scale ensured the stability of the material. Infusions of dried *V. vinifera* waste encapsulated with organic matrices at 50, 60, and 70 °C showed that the sensorial characteristics were influenced by the matrix used in the encapsulation. Physical–chemical parameters, and antioxidant activity of the preparations, depended on the grape variety. The encapsulation of by-products preserved the antioxidant capacity of the active compounds. No matrix altered the sensory characteristics of the infusions after two months. The infusions prepared at higher temperatures had better phenolic content and were more promising for use in human food, and the addition of honey made it more enjoyable [75].

Acid hydrolysis allowed for high crystallinity and the purification of cellulose from P. Noir grape pomace, and its cellulose crystals showed needle-shaped morphology, stability in aqueous dispersion after seven days of storage, and biocompatibility with human colon epithelial cells [67]. Grape pomace-loaded vesicles promoted cell proliferation, migration and reduced oxidative stress of keratinocytes and fibroblasts [23].

From the exposure, nanocarriers containing active substances from the grape pomace(s) may be allies in favor of human health since robustly investigated to prove safety and efficacy and improvements regarding the compounds in their free state.

## 5. The Use of Wine By-Products towards Sunscreen Development

By-product ingredients from the wine industry can elevate the sun protection factor (SPF) of sunscreens using different mechanisms, contributing to reducing the concentration of UV filters, that could be potentially harmful to the environment, decreasing the use of natural resources and, in parallel, adding value to compounds from renewable sources. The efficacy profile of these innovative formulations has been studied both via in vitro and in vivo tests by our research group [28,41,76].

Hübner and coworkers developed a sunscreen system containing UVA/B organic filters associated with 10.0% *w*/*w* of grape pomace (*V. vinifera* cv. C. Sauvignon). A significant increase was observed in the in vitro SPF value (172%) and antioxidant ability (710% in Trolox equivalents), in comparison to the extract-free formulation. Moreover, the study probed in vivo the photoprotective capacity of grape pomace. The sunscreen formulation containing pomace extract delayed by ~20% the appearance of the initial signs of erythema, compared to the control formulation [28].

Recently, the same research group reported the biocompatibility of two fractions of grape pomace (C. Sauvignon), chloroform (GPE-CHF), and ethyl acetate (GPE-EAF), using a fibroblast culture (NIH 3T3). When the cells were stressed with $H_2O_2$, an oxidative agent, the authors observed a cytotoxic effect from the GPE-CHF, whereas the ethyl acetate fraction (GPE-EAF) was non-cytotoxic in the used conditions. According to these findings, GPE-EAF (10.0% *w*/*w*) was associated with a mixture of UV filters, and the in vitro SPF was determined using a diffuse reflectance spectrophotometer with the integrated sphere as well the functional photostability. GPE-EAF increased the photoprotective efficacy by 66% and improved the photostability of the sunscreen system after 1 h of artificial UV exposure [76].

These studies are indicative of the potential of using extracts of winemaking residues in the development of sunscreens aligned with the challenges of sustainable development to face poverty, inequalities, and climate change.

## 6. Conclusions

The valorization of agro-industrial phytochemicals brings and highlights positive impacts for wine producers, consumers, and the environment. However, there are economic, technological, and agronomic challenges that require financial, human resources, infrastructure, and research investments to ensure the quality of green industrial production and zero waste through the circular economy. The choice and combined use of technologies can reduce costs, energy, and toxic solvents. In this context, various non-conventional technologies with different approaches for extraction, separation, and purification of actives from winery by-products have offered a viable and safer alternative with social, economic, and environmental balance. An effective partnership among different sectors of society responsible for the management and recycling of wine residues can intensify the resolution of disposal problems with eco-friendly, innovative technological solutions, and multiple high-value products. Thus, this present review found technological advances and promising biotechnological and nanotechnological applications of winemaking by-products for health promotion.

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