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VALORIZATION OF THE VITICULTURE WASTE IN THE NUTRACEUTICAL INDUSTRY

Teodora-Otilia ALEXIU, Laura-Dorina DINU

University of Agronomic Sciences and Veterinary Medicine of Bucharest,
Faculty of Biotechnologies, 59 Mărăști Blvd, District 1, 011464, Bucharest, Romania

Corresponding author email: laura.dinu@biotehnologii.usamv.ro

Abstract

The valorization of viticulture by-products (e.g., grapevine pomace and canes) in the nutraceutical industry represents a paradigm shift in sustainable resource management and innovation. Thus, recognizing the untapped potential within these residues, the nutraceutical industry has embraced them as valuable but less exploited raw materials. These wastes are characterized by a high polyphenolic composition with antimicrobial, antioxidant, anti-inflammatory, and cardioprotective effects, especially resveratrol, gallic acid, and proanthocyanidins. Therefore, this mini-review aims to update the potential of viticulture wastes for the production of polyphenol-rich nutraceuticals and nanoparticles used as bioactive molecule carriers. Additionally, the modulator effect of grape pomace on human and animal microbiota was highlighted. The viticulture waste valorization aligns with the principles of the circular economy while creating new revenue streams for wineries.

Key words*: viticulture waste, polyphenol-rich nutraceuticals, nanoparticles, gut microbiota modulation, circular economy.*

INTRODUCTION

Viticulture is a branch of the horticulture science that refers to the process of grapevine cultivation and harvesting grapes for consumption and wine production (vinification). Worldwide, four countries (France, Italy, Spain, and the United States) produce more than half the wine in the world. Romania is a significant wine-producing country with a long history of viticulture. It is the sixth-largest wine producer in Europe and is known for its diverse wine regions, indigenous grape varieties, and high-quality wines (World Wine Production Outlook, OIV Report). However, viticulture and vinification generate a significant amount of waste while managing by-products of vitivinicultural origin is a considerable challenge (D'Eusanio et al., 2023; Niculescu & Ionete, 2023). Therefore, appropriate waste management and valorization of these residues based on the circular economy principles are crucial and will have positive environmental, social, and economic effects.

Winemaking produces different by-products, mainly grape pomace or grape marc and wine lees that contain grape pulp, skins, seeds, stalks, shoots and dead yeast cells. The main subproduct is grape pomace, which is considered a pollutant for the environment and can be used as a supplement in animal feed, to obtain oil from grape seeds or be transformed into ethanol by distilleries (Bordiga et al., 2015). Also, viticulture generates a large quantity of plant remains, such as vine canes after pre-pruning and pruning operations, and leaves. These waste materials are often left in the vineyard to contribute to the organic matter content and improve soil conditions. However, this practice could have negative effects on soil microbiota and lead to the uptake of residual herbicides, pesticides, and heavy metals (Managing By-Products of Vitivinicultural Origin, OIV Report).

The chemical composition of viticulture waste is valuable, as it is rich in dietary fiber, polysaccharides, and a complex polyphenol mixture (Niculescu & Ionete, 2023; García-Lomillo et al., 2017; Bordiga et al., 2015). Traditionally considered waste, some of these by-products have recently gained attention for their potential applications in the nutraceutical industry. Nutraceutical products or foods have proved to induce important physiological benefits to human organisms, therefore these could be used to improve health, delay the

aging process, prevent chronic diseases, increase life expectancy, or support body structure or function.
This study aimed to review and update the research on the valorization of viticulture by-products in the nutraceutical industry, enhancing the interest in obtaining high-value functional ingredients. Thus, the work proved that the integration of viticulture waste into the development of health products could offer a compelling opportunity to merge sustainability with innovation in nutraceutical applications.

MATERIALS AND METHODS

The search was carried out in the available online databases (Web of Sciences, Scopus, Springer Link, Wiley, ScienceDirect, and Google Scholar) for studies involving grapevine waste valorization until March 2025.
The primary search keywords were “grapevine waste” (grape pomace, marc, seed, skin, stalk, vine stem, cane, shoot, trunk, and root), and “nutraceutical”. Other keywords used were “nanoparticles”, “fortified foods”, and “dietary supplements”. In the secondary search, the results were evaluated using a hierarchical approach based on the title, abstract, full manuscript, and relevance for the present review. Inclusion criteria based on publication characteristics were related to publication date (between 2000 and 2025), language of publication (English), and type of publication (mostly high-impact journals and peer-reviewed articles).

RESULTS AND DISCUSSIONS

The valorization of grape pomace in the nutraceutical industry

Grape pomace, a key winemaking residue, is rich in polyphenols such as flavonoids, anthocyanins, tannins, and phenolic acids, which exhibit strong antioxidant activity and can be utilized for their health-promoting properties (González-Centeno et al., 2013; Teissedre et al., 2000). Most of the studies concluded that red grape marc has a higher polyphenolic content compared to the pomace obtained from the white grape variety (Niculescu & Ionete, 2023; Onache et al., 2022). Also, the grape marc composition is influenced by terroir, climate, and winemaking technology (Onache et al., 2022). Grape seeds and skins are usually obtained from exhausted grape pomace, a product without alcoholic and tartaric constituents. Then, grape seeds are dried and pressed to extract oil, while the nonfat part can be used to produce flour rich in antioxidant proanthocyanidins (Dwyer et al., 2014; D’Eusanio et al., 2023). Based on bioactive molecule content, the nutraceutical industry has begun incorporating grape by-products into various functional foods, supplements, and cosmetic formulations.
Numerous studies have demonstrated the health benefits of bioactive compounds from grape-derived waste (pomace, seeds, skins), especially polyphenols. These compounds play a crucial role in reducing oxidative stress, a major contributor to chronic diseases such as cardiovascular disorders, diabetes, and neurodegenerative conditions (Rockenbach et al., 2011). The cardioprotective effects of grape pomace have been well documented, with studies indicating its ability to prevent the oxidation of low-density lipoprotein (LDL) cholesterol, a major factor in the development of atherosclerosis. Additionally, supplementation with grape pomace has been associated with an increase in LDL, further supporting cardiovascular health, but these effects depended on the content of grape marc in the diet and the feeding time (Bordiga et al., 2015; Almanza-Oliveros et al., 2024). Animal studies have also demonstrated that the consumption of red grape pomace reduces inflammatory markers such as tumor necrosis factor-alpha (TNF-α) and interleukin-10 (IL-10), leading to a decrease in size and number of atherosclerotic lesions (Taladrid et al., 2023). In addition to cardiovascular health, winemaking by-products show promise in regulating metabolic health and could help alleviate obesity-related inflammation and associated metabolic disorders. Polyphenolic compounds in grape pomace have been linked to improved glucose metabolism and insulin sensitivity, making them potential candidates for managing metabolic syndrome and diabetes (Taladrid et al., 2023). Also, these bioactive compounds exhibited anti-cancer effects (Martínez-Montemayor et al., 2010).

The health effects of nutraceutical Taurisolo®, a grape pomace polyphenol extract, containing resveratrol, quercetin, catechins, procianidins, gallic acid, and caffeic acid have been investigated by different works (Annunziata et al., 2019; Annunziata et al., 2021; Amato et al., 2024; Lapi et al., 2024). Tabel 1 shows the healthy benefits of the polyphenol-based nutraceutical formulation Taurisolo®, based on the published papers, clinical cases and case reports.

Table 1. The health benefits of the polyphenol-based nutraceutical formulation Taurisolo®

Biological effect		**References**
Antiviral	Bovine alphaherpesvirus 1 (BoAHV-1), causing infectious bovine rhinotracheitis	Cerracchio et al., 2023
	Herpes simplex virus (HSV)	Zannella et al., 2023
	COVID-19 Taurisolo® aerosol formulation Add-on therapy in the treatment of COVID-19 patients, based on both its anti-inflammatory and antioxidant effects Clinical trial	Zamparelli et al., 2022
Cardio vascular	L-arginine and Taurisolo® Blood pressure reduction Prevented microvascular damage from hypoperfusion-reperfusion	Lapi et al., 2024
	Diabetic patients with peripheral artery disease Clinical trial	Amato et al., 2024
	Prevent brain damage due to ischemia-reperfusion injury Rat model	Lapi et al., 2020
	Atheroslerosis Reduce both the serum levels of TMAO and oxidative stress-related biomarkers in humans Clinical trial	Annunziata et al., 2021
	Cardioprotective Reduce the toxicity induced by TMAO and high glucose concentrations Cell model	Lama et al., 2020
	Vascular protection Preserve the vascular function against ox-inflamm-ageing process and the consequent cardiovascular accidents Cell lines and clinical trial	Martelli et al., 2021
	Reduce TMAO Cross-over clinical trial	Annunziata et al., 2019a Annunziata et al., 2019b
	Antioxidant Human neutrophiles	Annunziata et al., 2021
Hepato protective	Reduce anabolic reactions Increase catabolic reactions, mitochondrial activity, promotes respiration and ATP production Liver cell model	Badolati et al., 2020

The study conducted by Annunziata et al. (2021) revealed the effect of this dietary supplement on serum levels of trimethylamine-N-oxide (TMAO), oxidized low-density lipoprotein (ox-LDL), and reactive oxygen species (D-ROMs), all of which are biomarkers linked to the development of atherosclerosis. The clinical trial, involving 213 participants divided into an active group and a placebo group, demonstrated that the administration of Taurisolo® over eight weeks resulted in a significant reduction in blood TMAO levels. The findings indicated a 49.78% decrease in TMAO levels after four weeks and a further reduction of 75.85% after eight weeks. Additionally, oxLDL levels dropped by 43.12% at the four-week mark and by 65.05% at the end of the study. Similarly, D-ROMs decreased by 34.37% and 49.68% after four and eight weeks, respectively (Annunziata et al., 2021). No significant changes were observed in the placebo group, reinforcing the efficacy of Taurisolo® as a potential nutraceutical intervention for cardiovascular risk reduction. These results suggest that grape-derived polyphenols may have protective effects by modulating oxidative stress and inflammation, both key factors in atherosclerosis progression (Annunziata et al., 2021). Recently, Amato et al. (2024) have proved that treatment with Taurisolo® reduced the damage of serum TMAO and exerts a protective effect on endothelial cells, thus the product might be used as an effective intervention to ameliorate peripheral artery disease symptoms (Amato et al., 2024). Lapi et al., 2024 have demonstrated in a murine model that L-arginine and polyphenol extract Taurisolo® maintained blood pressure levels within the physiological range and protected against microvascular injuries (Lapi et al., 2024). *In vitro* experiments suggested that Taurisolo® counteracts the toxicity induced by TMAO and high glucose concentrations, and may represent a useful nutraceutical approach for the prevention of cardiomyopathy in obese subjects (Lama et al., 2020). In mice, this nutraceutical has proved hepatoprotective effects because stimulated glucose uptake and reduced hepatic cholesterol and serum triglycerides (Badolati et al., 2020). The mechanism involved the reduction of anabolic reactions, such as the biosynthesis of cholesterol, bile acids, and plasma membrane lipids, while mitochondrial activity increased to promote respiration and ATP production (Badolati et al., 2020).

Furthermore, winemaking by-products possess potent antimicrobial properties, particularly against multidrug-resistant bacterial strains. The phenolic compounds found in grape seeds, skins, and stalks, such as flavonols, hydroxybenzoic acids, and stilbenes, have demonstrated bactericidal activity against Gram-positive and Gram-negative bacteria, including *Staphylococcus aureus*, *Escherichia coli*, and *Clostridium* species (Silva et al., 2018). These findings suggest that grape pomace extracts could serve as natural alternatives to synthetic antibiotics and food preservatives, addressing both public health and environmental concerns (Niculescu & Ionete, 2023). A recent study by Baroi et al. (2024) explores the green synthesis of silver nanoparticles (AgNPs) using grape pomace extracts from the native variety of Fetească Neagră, highlighting their potential antimicrobial and antioxidant applications (Baroi et al., 2024). Two extraction methods - classical temperature extraction and microwave-assisted extraction - were compared, with the latter yielding smaller, more stable nanoparticles with enhanced bioactivity. Results showed that the formation of AgNPs was performed in a relatively short period of time (96 h) and was influenced by the total phenolic content, while the best experimental variant involving the use of a 1:1 ratio (v/v, grape pomace extract: silver nitrate). Structural analysis of nanoparticles confirmed their crystalline nature through X-ray diffraction and morphological features via transmission electron microscopy (TEM). The antimicrobial activity of these nanoparticles was tested against *Staphylococcus aureus* ATCC 25923 and *Enterococcus faecalis* ATCC 29212, revealing significant bacterial inhibition for *S. aureus*, while showing no effect on *E. faecalis*, suggesting selective antibacterial properties. Additionally, antioxidant assays demonstrated superior free radical scavenging activity of AgNPs compared to raw grape pomace extracts (Baroi et al., 2024). Researchers concluded that the grape marc-derived AgNPs hold promise for nutraceutical and pharmaceutical applications, particularly in food preservation and antimicrobial treatments. Moreover, further work should optimize extraction methods to enhance nanoparticle efficacy and explore their broader biomedical applications (Baroi et al., 2024).

Additionally, grape pomace is a valuable source of dietary fiber, which supports gut health by promoting beneficial gut microbiota and enhancing digestive function (Dinu & Vamanu, 2024). In the case of grape marc, both phenolic compounds, and oligosaccharides promote bacterial growth, but most studies have not analyzed this effect separately. *In vitro* experiments, as well as some studies on livestock animals and humans have demonstrated the positive effects of grape pomace on beneficial bacterial taxa from gut microbiota (e.g., *Lactobacillus* spp. and *Bifidobacterium* spp.) (Gil-Sánchez et al., 2018; Chacar et al., 2018). In a mouse model, the administration of grape marc and seed extracts after antibiotic treatment showed a higher relative abundance of bacteria belonging to the Verrucomicrobiota and *Akkermansia* spp., which are linked to improved barrier function (Lu et al., 2019). Moreover, studies on animals proved that diets supplemented with grape pomace inhibited pathogen populations (*Campylobacter jejuni*, *E. coli*, and other Enterobacteriaceae) (Kafantaris et al., 2017; Kafantaris et al., 2018). A human trial with high-cardiovascular-risk subjects demonstrated that the cardiometabolic effects of grape pomace seasoning treatment were modulated by the human gut microbiota. In this case, the microbial changes in microbial composition, diversity, and functionality were correlated with reduced glycemia and decreased blood pressure (Taladrid et al., 2023).

A large number of studies explore the incorporation of grape-derive waste into functional foods, such as yogurt and meat products, to enhance their nutritional value and extend shelf life through natural antioxidant activity (López-Hernández et al., 2021). Grape marc extract has been used for the fortification of pork and chicken meat (burgers, sausages, loin marinade), yogurt, cheese, and chocolate (Marchiani et al., 2016; García-Lomillo et al., 2017; Darwish et al., 2023).

The valorization of other viticulture waste in the nutraceutical industry

Although most research focused on grape pomace valorization, more viticulture waste are rich in bioactive molecules. However, only a few studies examined eco-friendly approaches to repurpose these residues into high-value products, emphasizing their potential applications in pharmaceuticals, food industries, and bio-based materials.

Grape stalks represent almost 14% of the total weight of solid wine waste (Silva et al., 2021). Their composition includes lignocellulosic materials, tannins, as well as polyphenols (6% from dry weight). The main polyphenolic compounds are flavan-3-ols, flavonols, hydroxybenzoic acids (gallic and syringic acids), and stilbenes (Troilo et al., 2021). Similarly, vine canes have a rich polyphenolic profile, thus Escobar-Avello et al., 2019 identified a total of 75 compounds in canes from the Pinot Noir variety and revealed the presence of 17 polyphenols that were not previously described (Escobar-Avello et al., 2019). In another work, the most abundant phenolic compound class was stilbenoids, among the 44 phenolics identified (Escobar-Avello et al., 2021). Moreover, higher amounts of gallic acid with known antioxidant activity, were detected (Dorosh et al., 2020). Vine shoots are rich in polyphenols and lignocellulosic material and, thus were considered a promising substrate for lactic acid production (Bustos et al., 2007; Luque-Rodríguez et al., 2007).

Vine canes are rich in proanthocyanidins, stilbenes, and gallic acid. Therefore, the health-related potential of these viticulture by-products is particularly significant, given their abundance in bioactive compounds with antioxidant, anti-inflammatory, antimicrobial, and metabolic health-enhancing properties (Georgiev et al., 2014; Dinu & Vamanu, 2024). Moreover, it has been shown that important polyphenolic compounds from grape canes, resveratrol, and gallic acid can modulate gut microbiota (Chen et al., 2016; Iglesias-Carres et al., 2021).

The antimicrobial activity of vine stem extract has proved on *B. cereus*, *E. faecalis*, *L. monocytogenes*, *S. aureus*, *S. epidermidis*, and *K. pneumoniae* (Silva et al., 2018). Moreover, Bastos-Arrieta et al. (2018) explored the green synthesis of silver nanoparticles (Ag-NPs) using grape stalk waste extracts as a natural reducing and stabilizing agent (Bastos-Arrieta et al., 2018). This eco-friendly method leverages the polyphenols and reducing sugars in grape stalks to facilitate nanoparticle formation without the need for hazardous chemicals. The synthesis was optimized by varying pH, temperature, reaction time, and extract-to-metal solution ratio, with pH 4 and 6 yielding the most stable nanoparticles, averaging 27.7 ± 0.6 nm in size, as confirmed by TEM and scanning microscopy (SEM) imaging. Beyond their synthesis, these Ag-NPs were incorporated into screen-printed carbon nanofiber electrodes to enhance their electrochemical properties. The modified electrodes were evaluated for their ability to detect low levels of lead (Pb^{2+}) and cadmium (Cd^{2+}) ions in water samples. The results demonstrated high sensitivity and reproducibility, with detection limits of 2.7 μg/L for Pb^{2+} and 2.8 μg/L for Cd^{2+}, highlighting their potential for heavy metal detection in environmental monitoring (Bastos-Arrieta et al., 2018). This study underscores the sustainability of grape stalk waste-derived nanoparticles, showing their dual functionality in nanotechnology and environmental sensing applications.

CONCLUSIONS

The valorization of viticulture waste in the development of nutraceuticals represents a sustainable and innovative approach to addressing environmental challenges while leveraging the health-promoting potential of bioactive compounds. The high polyphenolic content of grape and vine-derived by-products underscores their value as functional ingredients to fortify foods, nutritional supplements, or microbiota modulators. The phenolic compounds, particularly resveratrol, gallic acid, and proanthocyanidins, exhibit antioxidant, anti-inflammatory, and antimicrobial activities, supporting their integration into formulations designed to prevent chronic diseases or to enhance human health. Future interdisciplinary research should focus on optimizing extraction and processing techniques to maximize the bioactivity and stability of polyphenolic compounds from these wastes, ensuring their long-term efficacy in health applications. Moreover, the utilization of viticulture and vinification waste aligns with circular economy principles, promoting resource efficiency and minimizing environmental impact. By repurposing these by-products into high-value health-related formulations, wineries can create new revenue streams while adopting sustainable waste management practices.

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