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SPECIAL ISSUE

Transforming winemaking waste: grape pomace as a sustainable source of bioactive compounds

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ABSTRACT

The valorisation of winemaking by-products has emerged as a sustainable approach to mitigate environmental challenges and promote resource efficiency within the wine industry. Grape pomace (GP), the primary solid residue generated during vinification, retains a substantial portion of the grape's polyphenols, representing a valuable source of natural antioxidants. Transforming this by-product into high-value bioactive ingredients holds significant potential for applications across the nutraceutical, food, and cosmetic industries.

This study investigated the phenolic composition and antioxidant capacity of GP from different grape varieties in the Rhône Valley area of France, including Alicante, Syrah, Mourvèdre, and Grenache. Total polyphenol content (TPC) was measured using the Folin–Ciocalteu method, while phenolic profiling—covering phenolic acids, flavonoids (flavan-3-ols, anthocyanins, flavonols) and stilbenes—was conducted using HPLC-DAD-ESI-QQQ. Antioxidant capacity was evaluated through DPPH, ABTS, FRAP, and ORAC assays.

The results revealed significant retention of phenolic compounds in GP following vinification, with concentrations ranging from 5–35 mg GAE/g DW depending on the sample type (GP skins or seeds). Fermented GP seeds, particularly from Syrah and Alicante varieties, displayed the highest phenolic content, rich in flavan-3-ol monomers and procyanidins, and exhibited superior antioxidant activity compared to GP skins across all vintages. Correlations between phenolic composition and antioxidant activity were explored to further elucidate the functional properties of bioactive compounds and identify the most promising GP extracts for further valorisation.

These findings highlight the potential of grape pomace as a readily available, low-cost source of polyphenolic compounds, supporting its conversion into bioactive extracts for a range of industrial applications.

KEYWORDS: grape pomace, phenolic compounds, antioxidant activity, sustainable valorisation, Macrowine 2025

INTRODUCTION

Grapevines (*Vitis vinifera* L.) represent a crop of major economic significance, with over 80 % of global grape production destined for wine production, yielding more than 258 million hectolitres annually (OIV, 2024). However, the winemaking process generates substantial quantities of by-products, primarily grape pomace (GP), wine lees, and wastewater, which pose environmental and economic challenges (Constantin *et al.*, 2024). Among these residues, GP is the most abundant, accounting for 20–30 % of the total grape weight processed during the winemaking process, which consists of residual skins, seeds, and in some cases also stems (Moutinho *et al.*, 2023). Traditionally treated as an agricultural waste, GP has been disposed of through practices such as composting, landfilling, or use as animal feed (Wang *et al.*, 2024). While these methods contribute to waste management, they can also lead to soil acidification, methane emissions, and water pollution, raising concerns about their environmental impact (Abreu *et al.*, 2024). Moreover, increasing awareness of sustainability challenges has driven interest in the valorisation of GP as a resource rather than a waste product.

GP is a rich source of bioactive compounds, such as polyphenols, dietary fibre, and unsaturated lipids, which makes it an attractive raw material for nutraceutical, pharmaceutical, food, and cosmetic applications (Caponio *et al.*, 2023). Notably, up to 70 % of the total phenolics present in grapes remain in GP post-vinification, contributing to its strong antioxidant and anti-inflammatory potential (Castello *et al.*, 2018; Panzella, 2020). Among these polyphenols, flavan-3-ols, and procyanidins—primarily concentrated in grape seeds and skins—are the most abundant, representing up to 50 % of GP's total phenolic content and contributing significantly to its bioactivity (Rockenbach *et al.*, 2011; Valencia-Hernandez *et al.*, 2021). Anthocyanins, responsible for the red pigmentation of grapes and wines, are also retained in grape skins to varying extents depending on the grape variety and winemaking conditions, further enhancing GP's functional potential as a source of natural pigments and antioxidant agents (Castellanos-Gallo *et al.*, 2022).

Other key phenolic classes present in GP include phenolic acids, valued for their antioxidant and biological activities (Kumar & Goel, 2019), and flavonols, which, although present in lower concentrations, contribute to plant defence mechanisms (Azman *et al.*, 2022). Stilbenes, a minor class of non-flavonoid polyphenols, account for approximately 1 % of GP's total polyphenol content but are widely studied for their health-promoting properties (Németh *et al.*, 2017). However, GP's phenolic composition is highly variable, influenced by grape variety, vinification techniques, and environmental conditions, which collectively shape its bioactive potential and determine its optimal applications (Karastergiou *et al.*, 2024).

In recent years, the valorisation of GP has attracted increasing interest as part of a broader effort to transition the wine industry towards a circular economy. In addition to addressing waste management challenges, the recovery of bioactive compounds from GP offers significant potential for the development of high-value, phenolic-rich extracts with potential health benefits (Ferri *et al.*, 2020; Sodhi *et al.*, 2024). Recent research has focused on evaluating the functional properties of GP derived from various grape varieties, particularly its antioxidant capacity and biological activities. In vitro assays, such as DPPH, ABTS, FRAP, and ORAC, have consistently demonstrated the potent antioxidant potential of GP extracts (Cañadas *et al.*, 2023; Radulescu *et al.*, 2024). Additionally, biological models have further elucidated the anti-inflammatory and protective effects of these extracts (Bocsan *et al.*, 2022; Calabriso *et al.*, 2022; Chedea *et al.*, 2022).

Despite growing evidence supporting the antioxidant and bioactive potential of GP extracts, further research is needed to better characterise their phenolic composition and functional properties, particularly given the variability associated with grape variety and terroir. In this framework, this study aims to characterise the phenolic composition and antioxidant properties of GP derived from red grape varieties cultivated in the Rhône Valley, France. By investigating the relationships between phenolic content and antioxidant capacity, this research not only aims to deepen the scientific understanding of GP's functional potential but also to identify the most promising grape varieties for the development of bioactive extracts, supporting their industrial valorisation and contributing to sustainable resource utilisation within the winemaking industry.

MATERIALS AND METHODS

1. Chemicals

Water was purified using a Milli-Q system (Millipore, Guyancourt, France). Standards of malvidin-3-*O*-glucoside, quercetin, myricetin, and kaempferol were obtained from Extrasynthese (Genay, France), and standards of catechin, gallic acid and *trans*-resveratrol from Sigma-Aldrich (Milan, Italy). *Trans*-piceid, piceatannol, and *trans*-ε-viniferin were isolated from grapevine shoots in the MIB group of the ISVV. Folin–Ciocalteu phenol reagent, sodium carbonate, 1,1-diphenyl-2-picrylhydrazyl (DPPH), Trolox, fluorescein, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS), potassium persulfate, sodium acetate trihydrate, TPTZ (2,4,6-tris(2-pyridyl)-s-triazine), ferric chloride hexahydrate, ferrous sulfate heptahydrate, AAPH (2,2′-azobis(2-amidinopropane) dihydrochloride), disodium hydrogen phosphate and sodium dihydrogen phosphate were purchased from Sigma-Aldrich (Milan, Italy). Methanol and formic acid of LC-MS grade, acetonitrile (HPLC grade), as well as hydrochloric, acetic, and formic acid, were obtained from Fisher Chemical (Illkirch, France). Ethanol, methanol, and acetone of technical grade were purchased from VWR International (Pessac, France).

2. Grape Pomace Samples

GP from *Vitis vinifera* L. cultivars Grenache (GRE), Syrah (SYR), and Alicante (ALI) from the 2021–2023 vintages, as well as Mourvèdre (MOU) from the 2022 and 2023 vintages, were used in this study. All samples were collected from the Rhône Valley region (Châteauneuf-du-Pape appellation). After vinification, GP was mechanically separated into skins and seeds, yielding two distinct fractions. The GP seed fraction contained approximately 60–80 % of seeds, with the remainder consisting of skins and other vinification residues. Similarly, the GP skin fraction comprised 60–80 % of skins, with the rest consisting of seeds and residual vinification materials. The GP samples were analysed and processed as received from the winery to accurately represent their potential as raw materials for industrial applications.

3. Grape Pomace Sample Preparation

GP was lyophilised, and the dried material was finely ground using a ball mill prior to extraction. Polyphenol extraction was performed in duplicate following a previous method (Ky *et al.*, 2014). Briefly, 6 g of dried GP powder was extracted with 55 mL acetone/water (70:30, *v/v*) for 4 h in the dark at room temperature. The remaining solid residue underwent a second extraction with 55 mL methanol/water (60:40, *v/v*) for 2.5 h under the same conditions. The resulting supernatants were collected by centrifugation, combined, and concentrated to dryness under reduced pressure at 30 °C to remove solvents. The crude extracts were then reconstituted in water, freeze-dried, and subsequently analysed for total phenolic content (TPC), antioxidant activity, and phenolic composition by HPLC-DAD-ESI-QQQ.

4. Grape Pomace Anthocyanin Extraction

Anthocyanins were extracted from GP skins in duplicate, following a previous protocol (Ky *et al.*, 2014). 1 g of dried GP skin powder was sequentially extracted four times with acidified methanol (40 mL, 0.1 % HCl in methanol) under the following conditions: 4 h, 12 h, 4 h, and 12 h at room temperature. Supernatants from each extraction were pooled and evaporated to dryness under reduced pressure at 30 °C to remove solvents. The dried extracts were reconstituted in water, freeze-dried, and subsequently analysed for anthocyanins by HPLC-DAD

5. Determination of Total Polyphenol Content (TPC)

The total phenolic content (TPC) of GP extracts was determined using the Folin–Ciocalteu assay (Singleton *et al.*, 1999). Crude extracts were solubilised in a water/ethanol mixture (1:1, *v/v*) at concentrations appropriate for each extract type (0.5 g/L for GP skins and 0.25 g/L for GP seeds). For the assay, 20 µL of the extract was mixed with 100 µL of 10-fold diluted Folin–Ciocalteu reagent and 80 µL of sodium carbonate solution (7.5 %). The mixture was incubated for 30 min at room temperature in the dark. Absorbance was then measured at 760 nm using a FLUOstar Omega microplate reader (BMG Labtech) at 25 °C. A calibration curve with gallic acid (0–200 mg/L) was used to quantify the polyphenol content in the samples. TPC was expressed as mg of gallic acid equivalents (GAE) per gram of dry weight (DW) of GP.

6. Antioxidant Assays

6.1. DPPH Assay

The GP solutions prepared for the Folin assay (section 5) were also used for the DPPH assay. 10 µL sample was mixed with 190 µL of freshly prepared DPPH solution (200 µM in methanol) and incubated for 30 min at room temperature. The absorbance of the resulting mixture was measured at 515 nm using an automated microplate reader. Trolox served as the calibration standard, with concentrations ranging from 0 to 1.5 mM, and results were expressed as µmol Trolox equivalents per gram of DW.

6.2. Ferric Reducing Antioxidant Potential (FRAP) Assay

The GP solutions prepared for the Folin assay (section 5) were also used for the FRAP assay. The FRAP reagent was freshly prepared each day by combining 100 mL of 300 mM sodium acetate buffer (pH 3.6), 10 mL of 10 mM TPTZ solution, and 10 mL of 20 mM ferric chloride. A calibration curve was generated using varying concentrations of Trolox (0–1.5 mM). Samples (10 µL) were incubated with 190 µL of FRAP reagent for 30 min in the dark. The FRAP assay was carried out using an automated plate reader set to measure absorbance at 593 nm. Results were expressed as µmol Trolox equivalents per gram of DW.

6.3. ABTS Assay

The GP solutions prepared for the Folin assay (section 5) were also used for the ABTS assay. The ABTS radical cation solution was prepared by mixing 2.45 mM potassium persulfate with 7 mM ABTS and incubating the mixture in the dark at room temperature for 12–16 h. Prior to use, the $ABTS^{+\bullet}$ solution was diluted with Milli-Q water to achieve an absorbance of 0.70 ± 0.02 at 734 nm, measured using an automated microplate reader. Samples (10 µL) were then combined with 190 µL of the $ABTS^{+\bullet}$ solution and allowed to react for 30 min. Radical scavenging capacity was determined using a Trolox calibration curve (0–1.25 mM), and results were expressed as µmol Trolox equivalents per gram of DW.

6.4. Oxygen Radical Absorbance Capacity (ORAC) Assay

GP extracts were dissolved in water/ethanol (1:1, *v/v*) at 5 mg/L (for both GP skins and seeds). The ORAC assay was performed using an automated microplate reader equipped with a fluorescence detector, with excitation and emission wavelengths set at 485 nm and 530 nm, respectively. The analysis was conducted in a phosphate buffer (pH 7.4, 75 mM). Peroxyl radicals were generated using 40 mM AAPH, and fluorescein (117 nM) was used as the substrate. Measurements were taken every minute for 90 min at 37 °C. ORAC values were calculated based on a Trolox calibration curve (0–40 µM) and expressed as µmol Trolox equivalents per gram of DW.

7. HPLC-DAD-ESI-QQQ Analysis of Phenolic Compounds

GP extracts were analysed using HPLC coupled with a diode-array detector (DAD) and a Triple Quadrupole Mass Spectrometer (QQQ) following the modified method of (Gadrat *et al.*, 2021) to optimise separation and detection. The HPLC system (Agilent 1200 Infinity series) was equipped with a Kinetex C18 column (150 × 3 mm, 2.6 µm, Phenomenex), operated at a flow rate of 0.4 mL/min with a 10 µL injection volume.

Extracts were prepared by dissolving samples in acidified water (0.1 % formic acid) and methanol (1:1, *v/v*), with concentrations of 2 g/L for GP skins and 0.4 g/L for GP seeds. Prior to injection, all samples were filtered through a 0.45 µm membrane. Separation was performed using a binary solvent system: solvent A (0.1 % formic acid in water) and solvent B (0.1 % formic acid in methanol). The gradient of eluent B was adapted as follows: 2% from 0 to 2 min, 2 to 20 % from 2 to 5 min, 20 to 40 % from 5 to 25 min, 40 to 60 % from 25 to 38 min, 60 to 80 % from 38 to 43 min, 80 to 98 % from 43 to 51 min, 98 to 2 % from 51 to 52 min, 2 % from 52 to 55 min. The column was equilibrated for 4 min between injections.

Phenolic compounds were quantified using a 6460 Triple Quadrupole Mass Spectrometer (Agilent Technologies, Waldbronn, Germany) with heated electrospray ionisation (ESI), operating in both positive and negative ionisation modes. Calibration curves were established with pure standards of catechin, gallic acid, *trans*-resveratrol, *trans*-ε-viniferin, *trans*-piceid, piceatannol, quercetin, kaempferol, and myricetin, prepared in solvent A/methanol (1:1, *v/v*), at concentrations ranging from 0.05 to 10 mg/L. Phenolic compounds with available reference standards were quantified using their respective calibration curves. Flavan-3-ols and procyanidin dimers were quantified as µg of catechin equivalents per gram DW, phenolic acids as µg of gallic acid equivalents per gram DW, and quercetin glycosides as µg of quercetin equivalents per gram DW. Data processing was carried out using MassHunter Qualitative Analysis software (Agilent Technologies).

8. HPLC-DAD Analysis of Anthocyanins

GP skin extracts were dissolved in acidified water (0.1 % formic acid) and methanol (50:50, *v/v*) at a concentration of 10 g/L, filtered through a 0.45 µm membrane, and 20 µL was injected into a Thermo Scientific HPLC system (Thermo Fisher Scientific, Waltham, MA, USA) equipped with an Accela 600 pump module and a UV-Visible DAD, following the method by (González-Centeno *et al.*, 2017). Chromatographic separation was performed using a reverse-phase C18 Nucleosil column (250 × 4.0 mm, 5 µm). All samples were analysed in triplicate and anthocyanins were monitored at 520 nm, identified by comparison with external standards, and results were expressed as µg of malvidin-3-*O*-glucoside equivalents per gram DW of GP skins. Data processing was carried out using the XCalibur software (Thermo Scientific).

9. Statistical Analysis

Statistical analyses were conducted using RStudio (version 4.4.2). Two-way ANOVA ($a = 0.05$) was used to assess significant differences, followed by Tukey's HSD test for pairwise comparisons. Spearman correlation and principal component analysis (PCA) were performed to explore relationships between antioxidant capacity and phenolic composition.

RESULTS AND DISCUSSION

1. Total Phenolic Content (TPC)

The TPC of GP skins and seeds, determined using the Folin–Ciocalteu method, is presented in Figure 1. Significant differences were observed across all samples ($p < 0.05$), demonstrating the variability in polyphenol content due to both grape variety and vintage effects.

Among all samples, Syrah 2023 skins, Alicante 2021 and 2023 skins, and Grenache 2021 seeds exhibited the highest TPC, with values close to or exceeding 30 mg GAE/g DW. Notably, Syrah 2023 and Alicante 2023 seeds also presented

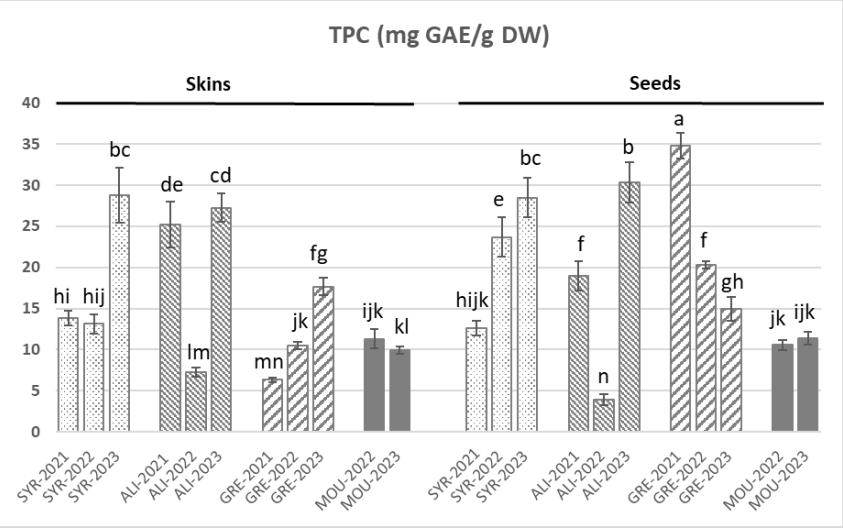


FIGURE 1. Total Phenolic Content (TPC) of GP skins and seeds.

SYR: Syrah, ALI: Alicante, GRE: Grenache, MOU: Mourvèdre. Letters indicate significant differences between GP samples with $\alpha = 0.05$.

high phenolic content, reinforcing the trend of these varieties displaying elevated TPC levels. In contrast, the lowest TPC values were observed in Alicante 2022 skins and seeds, as well as Mourvèdre 2022 and 2023 skins and seeds, with values around 10 mg GAE/g DW or below.

Despite vintage-related fluctuations, some consistent trends emerged. Alicante skins and seeds exhibited high TPC values in both 2021 and 2023, while a marked decline was observed in 2022. This notably low TPC in 2022 may be attributed to environmental factors, winemaking practices, or intrinsic differences in the initial polyphenol content of the grapes, reflecting variations in grape composition and polyphenol biosynthesis (Azaroual *et al.*, 2021). Syrah maintained relatively elevated TPC values in both skins and seeds across all years, with a notable peak in 2023. In contrast, Mourvèdre displayed low TPC values in both skins and seeds regardless of the year. Grenache seeds, particularly in 2021, stood out with significantly higher phenolic content compared to the corresponding skins, indicating a pronounced concentration of phenolics in the seed fraction for this variety.

These results underscore the significant influence of both varietal traits and vintage on phenolic content. While some samples maintained consistently high levels across years, others exhibited notable variability, reflecting the interplay between genetic factors and environmental conditions. These findings align with previous research on the phenolic diversity of red GP (Da Porto *et al.*, 2015; de la Cerda-Carrasco *et al.*, 2015; Ky & Teissedre, 2015).

2. Antioxidant capacity

The antioxidant capacity of GP extracts was evaluated using DPPH, ABTS, FRAP, and ORAC assays (Figure 2), which assess radical scavenging activity (DPPH, ABTS), reducing power (FRAP), and peroxyl radical scavenging capacity (ORAC). Despite methodological differences, all assays revealed consistent trends across varieties, and vintages, closely reflecting the variations observed in TPC.

In general, GP seeds demonstrated higher antioxidant activity than skins, in agreement with previous studies (Guaita *et al.*, 2023). The results were again influenced by vintage, yet distinct patterns emerged. Grenache 2021 seeds displayed outstanding antioxidant capacity, particularly in the ORAC and ABTS assays, with values exceeding 1200 and 400 µmol Trolox eq./g DW, respectively. This trend was further supported by the FRAP and DPPH assays, (300 µmol Trolox eq./g DW for FRAP and 400 µmol Trolox eq./g DW for DPPH).

Additionally, Alicante (2021 and 2023), Syrah 2023 skins and seeds, and Grenache 2022 seeds were highly active. These extracts consistently demonstrated strong antioxidant capacity, with ORAC values ranging from 600 to 800 µmol TE/g DW, and DPPH, ABTS, and FRAP results between 200 and 400 µmol TE/g DW, underscoring their potent antioxidant activity across various assay methods.

In contrast, Mourvèdre 2022 and 2023, along with Alicante 2022, consistently showed the lowest antioxidant activity in all tests, with ORAC values below 200 µmol Trolox eq./g DW, and equally low results for the other assays. These lower

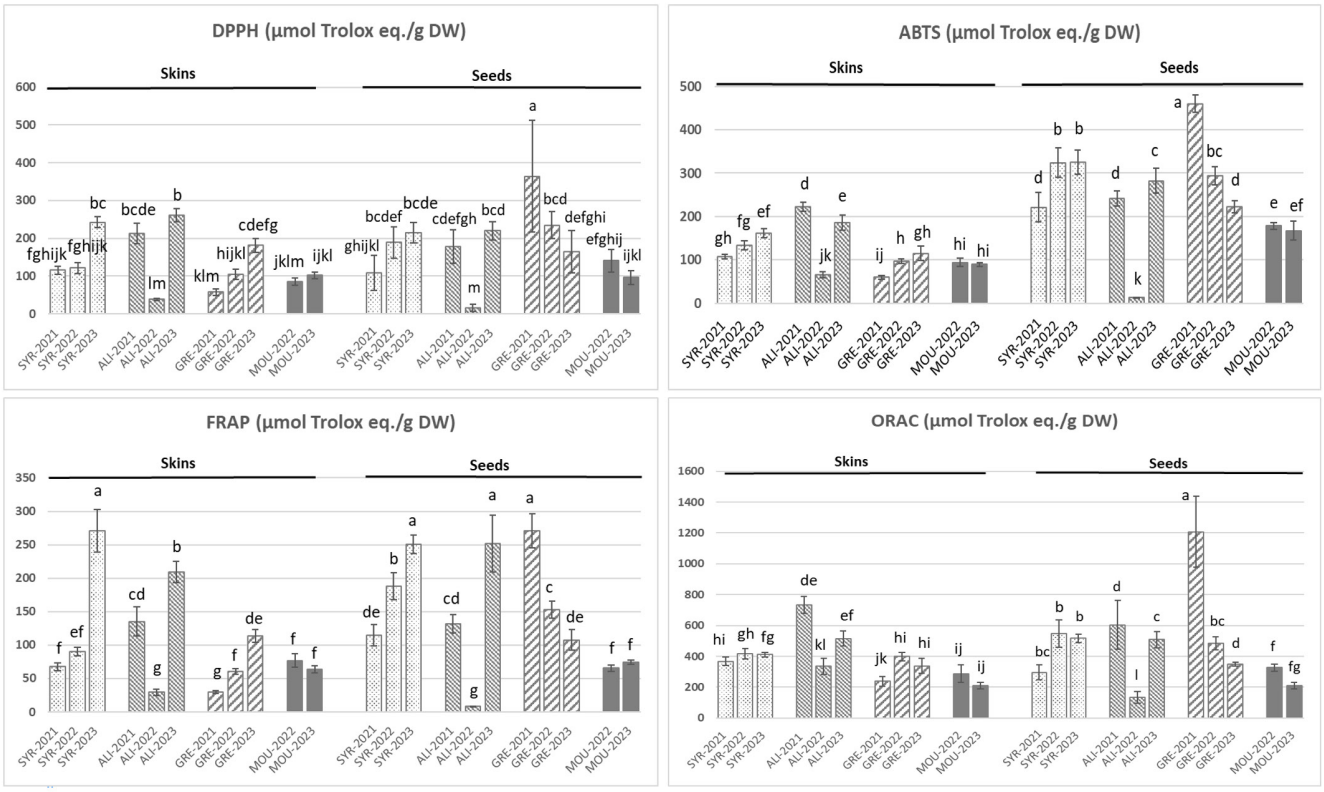


FIGURE 2. Antioxidant capacity (DPPH, ABTS, ORAC, FRAP) of GP skins and seeds.

SYR: Syrah, ALI: Alicante, GRE: Grenache, MOU: Mourvèdre. Letters indicate significant differences between GP samples with $\alpha = 0.05$.

values align with the TPC data, indicating a reduced capacity for radical scavenging and reducing activity in these samples.

While inter-annual variability was evident, certain samples—such as Grenache 2021 seeds and Syrah 2023—consistently exhibited high antioxidant activity across vintages and assays, indicating a particularly strong antioxidant profile. Similar patterns in the in vitro antioxidant activity of GP have been reported in other grape varieties, including Negramaro (Gerardi *et al.*, 2021), Cabernet franc (Moro *et al.*, 2021), Aglianico (Crescente *et al.*, 2023), Cabernet-Sauvignon *(Daniela et al., 2024; de Campos et al.,* 2008) and Merlot (Yammine *et al.*, 2020).

3. Phenolic composition of GP skins and seeds

Figure 3 illustrates the targeted phenolic content (flavan-3-ols, procyanidin dimers, flavonols, stilbenes, and phenolic acids) in GP skins and seeds across the 2021–2023 vintages, expressed in µg/g DW. Detailed quantification of the individual phenolic compounds is provided in Tables S1–S3.

Figure 4 presents the anthocyanin content in GP skins, across all studied vintages, whereas Table S4 provides a breakdown of the individual anthocyanins.

3.1. Flavan-3-ols, procyanidins, phenolic acids, flavonols, and stilbenes

Phenolic compounds play a crucial role in grape physiology and significantly contribute to the composition and bioactivity of GP (Almanza-Oliveros *et al.*, 2024). The main flavan-3-ols, procyanidin dimers, flavonols, stilbenes, and phenolic acids present in GP were characterised using HPLC-DAD-ESI-QqQ. The results revealed distinct profiles in both concentrations and phenolic distribution for GP skins and seeds, as shown in Figure 3.

Notably, GP skins exhibited a more diverse phenolic profile compared to seeds, with significant contributions from flavan-3-ols, procyanidin dimers, flavonols, phenolic acids, and stilbenes. In contrast, seeds contained higher overall phenolic concentrations, primarily composed of flavan-3-ols and procyanidin dimers. The presence of flavonols and stilbenes in seeds is mainly attributed to the heterogeneous nature of GP samples, as described in Section 2 (Materials and methods). Additionally, the partial extraction of these compounds during vinification, facilitated by maceration, may have contributed to their release into the fermenting must.

Among GP skins, Syrah (2023) exhibited the highest phenolic concentrations, primarily due to elevated flavan-3-ol and procyanidin levels. Alicante from the 2021 and 2023 vintages followed, with concentrations exceeding 1000 µg/g DW. In contrast, Grenache and Mourvèdre skins consistently showed lower total phenolic contents, around 500 µg/g DW across all vintages (Figure 3).

Syrah, particularly in the 2023 vintage, exhibited higher concentrations of flavan-3-ols and procyanidin dimers

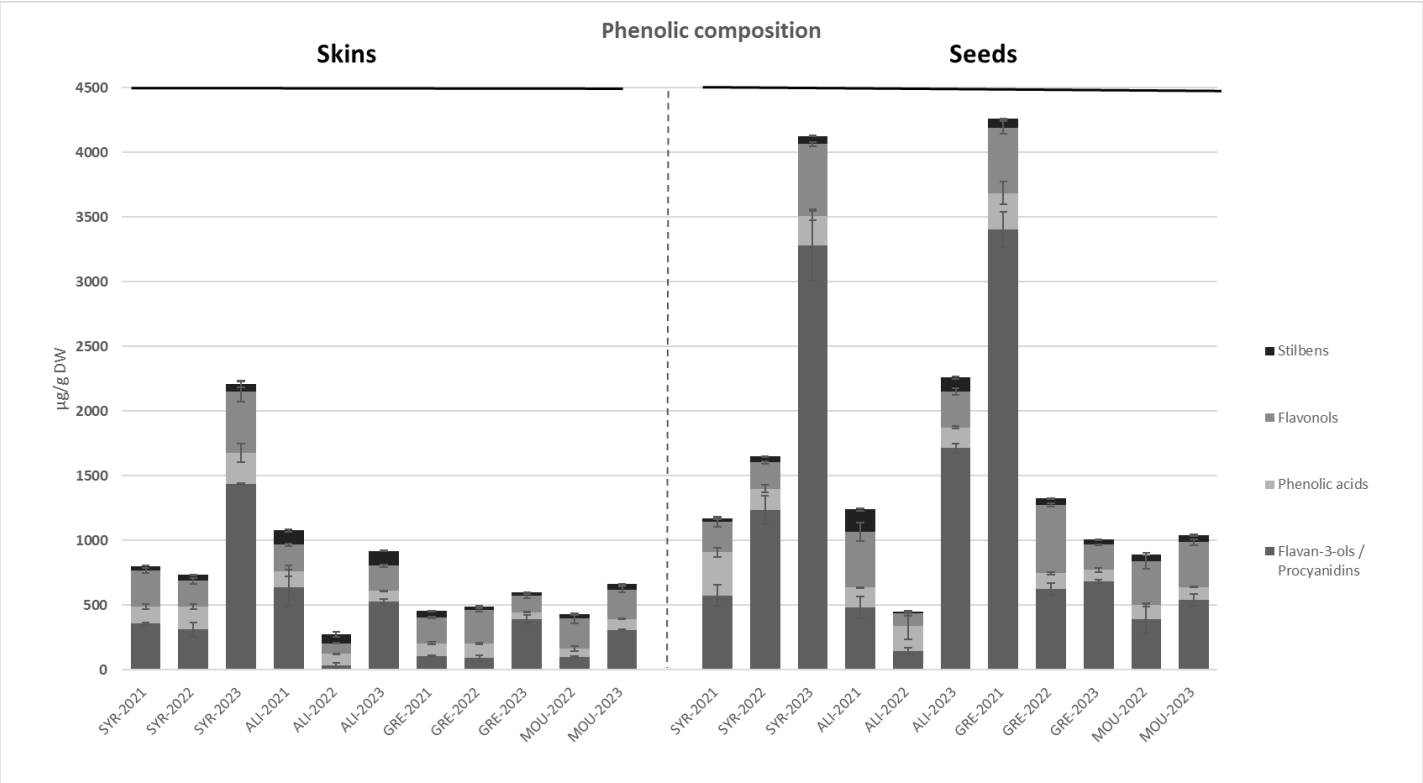


FIGURE 3. Phenolic composition of GP skins and seeds extracts.

SYR: Syrah, ALI: Alicante, GRE: Grenache, MOU: Mourvèdre. Flavan-3-ols/procyanidin dimers: µg catechin eq. per g of DW; Phenolic acids: µg gallic acid eq. per g of DW; Flavonols: quercetin and quercetin glycosides as µg quercetin eq. per g of DW; other flavonols: µg of their corresponding standards per g of DW; Stilbenes: µg of their corresponding standards per g of DW.

compared to other varieties. Notably, epicatechin gallate levels remained consistently elevated across all vintages. Regarding phenolic acids, Syrah also showed the highest concentrations, with gallic acid and syringic acid levels being particularly prominent and exceeding those of other varieties. Syringic acid is of particular interest due to its biological activity and prevalence in wine by-products (Panzella, 2020). Its elevated levels in GP have been previously reported (Meini *et al.*, 2019). Additionally, flavonol concentrations remained relatively stable across varieties; however, Syrah skins, particularly from the 2023 vintage, exhibited significantly higher levels. Syrah has been previously recognised for its high phenolic content *(de Andrade et al., 2021; González-Centeno et al.,* 2014; Spissu *et al.*, 2022). Despite the influence of vintage, the overall elevated phenolic content of this variety may contribute to its superior antioxidant activity, as discussed in Section 2.

Stilbenes, present in low concentrations across all samples, were most abundant in Alicante skins, with levels ranging from 69.9 to 116.6 µg/g DW. Other GP skins contained less than 60 µg/g DW. Notably, stilbene content in Alicante grapes or GP has not been previously reported, making this finding significant for understanding the unique phenolic profile and potential bioactive properties of this variety. Although the stilbene composition of GP remains relatively unexplored, our results align with previous reports on *trans*-resveratrol content in Syrah GP (de Andrade *et al.*, 2021), *trans*-piceid in Tempranillo GP (Loarce *et al.*, 2020) and piceatannol in Malbec GP (Antoniolli *et al.*, 2015).

In GP seeds, flavan-3-ols and procyanidin dimers were the dominant phenolic compounds, in accordance with previous studies (Guaita *et al.*, 2023; Maier *et al.*, 2009). Syrah and Alicante, particularly in the 2023 vintage, along with Grenache (2021), exhibited the highest phenolic concentrations, ranging from 2000 to 4000 µg/g DW (Figure 3). In contrast, Grenache (2022 and 2023) and Mourvèdre (2022 and 2023) seeds had lower phenolic contents, around 1000 µg/g DW, while Alicante (2022) seeds showed the lowest levels, mirroring the trend observed in Alicante 2022 skins and aligning with TPC results (see Section 1).

Other phenolic families were present in lower concentrations in GP seeds. Notably, Alicante (2021) seeds contained the highest stilbene levels detected (172.2 µg/g DW), likely resulting from the heterogeneous nature of GP samples or the transfer of these compounds during vinification. Overall, phenolic composition exhibited strong vintage-dependent variations, preventing the identification of consistent trends. However, Syrah, Alicante, and Grenache seeds consistently displayed the highest phenolic levels.

3.2. Anthocyanins

The major anthocyanins in GP skins were characterised using HPLC-DAD analysis. Although small amounts may be present in GP seeds due to the vinification process and the inherent variability of GP samples (see Section 2, Materials and methods), quantification was performed exclusively on skins, as they constitute the primary source of these pigments.

Figure 4 illustrates the anthocyanin composition of GP skins, revealing substantial differences across grape varieties and vintages. Anthocyanins were predominantly present

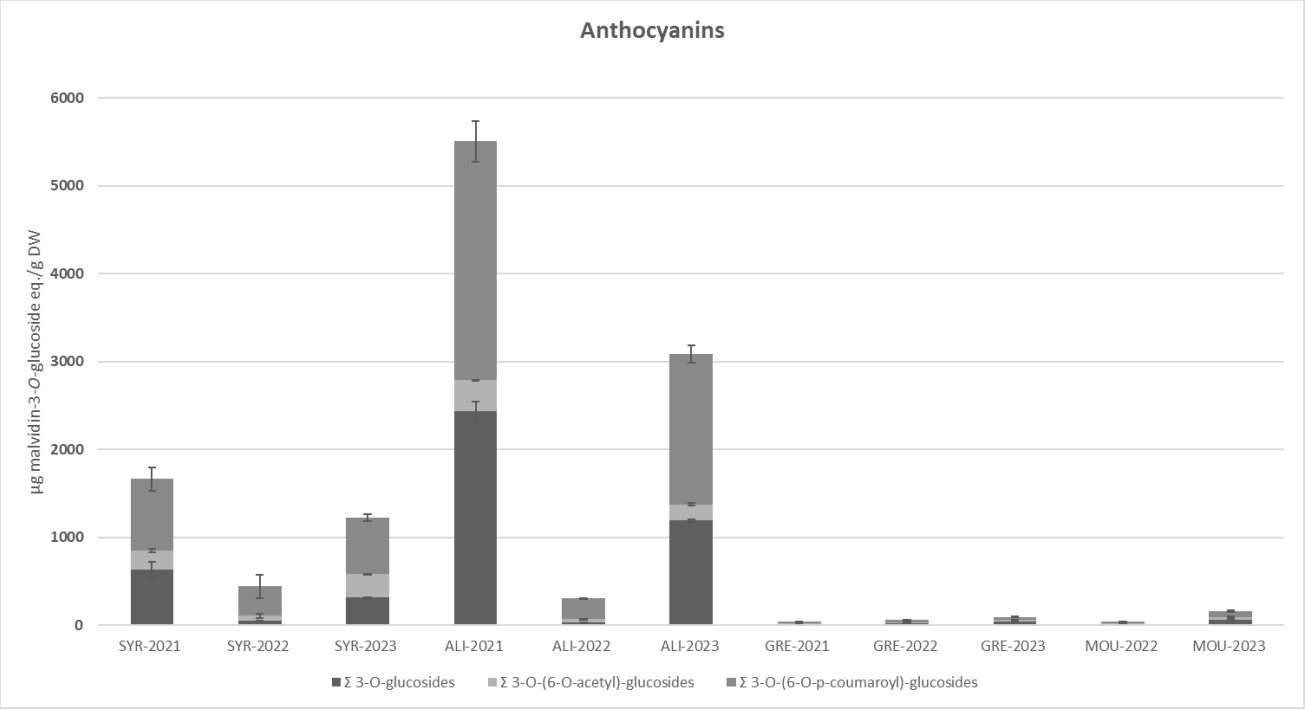


FIGURE 4. Anthocyanins in GP skin extracts.

SYR: Syrah, ALI: Alicante, GRE: Grenache, MOU: Mourvèdre. Anthocyanins are expressed as µg malvidin-3-*O*-glucoside eq. per g of GP skins DW

as 3-*O*-glucosides, followed by 3-*O*-(6-*O*-*p*-coumaroyl)-glucosides and 3-*O*-(6-*O*-acetyl)-glucosides, consistent with previous findings on red GP (Loarce *et al.*, 2021; Oliveira *et al.*, 2015). Alicante GP skins exhibited the highest anthocyanin content, reaching up to 5000 µg/g DW, with 3-O-glucosides as the dominant forms. This trend was particularly evident in the 2021 and 2023 vintages, whereas Alicante 2022 showed significantly lower levels, in line with its reduced TPC and overall phenolic composition. As a teinturier variety, Alicante is well known for its high anthocyanin content, particularly malvidin-3-*O*-glucoside, which contributes to its intense pigmentation and strong antioxidant properties (Revilla *et al.*, 2013).

Syrah skins contained lower anthocyanin concentrations than Alicante, reaching a peak of approximately 2000 µg/g DW in 2021. A decline in 2022 suggests that environmental or viticultural factors may have influenced their levels. Although Syrah is widely recognised for its high anthocyanin content, its concentrations can vary depending on cultivation conditions, winemaking processes, and extraction techniques (de Oliveira *et al.*, 2019a; de Oliveira *et al.*, 2019b). Notably, the relative proportions of 3-*O*-glucosides and 3-*O*-(6-*O*-*p*-coumaroyl)-glucosides were similar in both Alicante and Syrah. Grenache and Mourvèdre GP skins consistently exhibited the lowest anthocyanin levels, with values below 500 µg/g DW, underscoring the strong varietal influence on anthocyanin accumulation, as reported in the literature (Kallithraka *et al.*, 2005). Additionally, pronounced variations across vintages highlight the impact of environmental factors—such as temperature fluctuations, UV exposure, and water availability—on anthocyanin biosynthesis, which are known to affect phenolic metabolism in grapes (He *et al.*, 2010).

4. Correlations between phenolic composition and antioxidant activity

A correlation analysis was performed to investigate the relationships between phenolic composition and antioxidant capacity in GP. Spearman's test was used to assess associations between variables, and Principal Component Analysis (PCA) was conducted to identify patterns in the data, highlighting GP extracts with potential for further investigation and application based on their distinct phenolic profiles and antioxidant activity.

4.1. Spearman correlation

Figure 5 presents the Spearman correlation matrix, where deeper green circles indicate stronger positive correlations ($r > 0.5$). Strong positive correlations were observed between antioxidant assays (DPPH, ABTS, FRAP, ORAC), with values exceeding 0.7, confirming their close interrelation. As expected, TPC exhibited robust correlations with all antioxidant assays ($r > 0.8$), consistent with previous findings (Dudonné *et al.*, 2009).

Flavanols and procyanidin dimers, which are particularly abundant in grape seeds, showed strong correlations with both TPC and antioxidant assays. This supports their key role in determining the bioactivity of GP extracts, in line with previous studies (Dabetic *et al.*, 2022; Guaita *et al.*, 2023; Maier *et al.*, 2009). In contrast, flavonols and phenolic acids exhibited lower to moderate correlations with ABTS and FRAP assays, suggesting a more limited contribution to antioxidant capacity compared to flavan-3-ols and procyanidin dimers.

Stilbenes, despite their well-documented antioxidant potential (Aja-Perez *et al.*, 2021; Biais *et al.*, 2017), did not correlate with TPC or antioxidant assays, likely due to their relatively low concentrations in GP. Furthermore, the observed trends may reflect the combined effects of stilbene compounds, as individual stilbenes may vary in antioxidant capacity. This could explain why high-stilbene grape varieties, such as Alicante, did not show a clear correlation with antioxidant activity. The contribution of stilbenes may also depend on structural differences, redox potential, or synergistic interactions with other phenolics, which bulk antioxidant assays may not fully capture. Similarly, anthocyanins did not show a significant correlation with antioxidant capacity, most likely due to their low presence in GP seeds. Nevertheless, given their strong antioxidant properties (Bitsch *et al.*, 2004; Sabra *et al.*, 2021), anthocyanins would be expected to play a more prominent role in matrices where they are more abundant, such as grape skins.

4.2. Principal Component Analysis (PCA)

In Figure 6, PCA results revealed distinct patterns in the phenolic composition and antioxidant capacity of GP samples, with Principal Component 1 (PC1) explaining 61.5 % of the total variance. This component was primarily driven by total phenolic content (TPC), flavanol monomers, procyanidin dimers, and antioxidant assays. Principal Component 2 (PC2), accounting for 17.67 % of the variance, was mainly influenced by anthocyanins and stilbenes, further highlighting varietal differences.

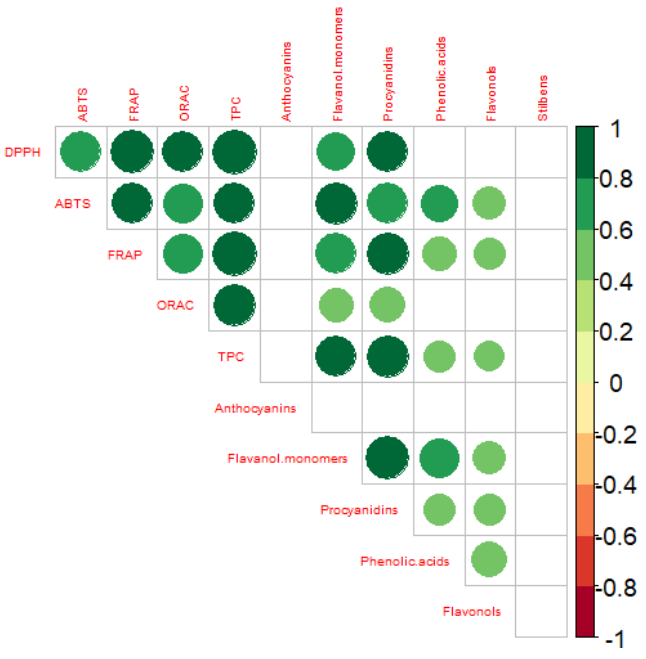


FIGURE 5. Spearman correlation matrix.

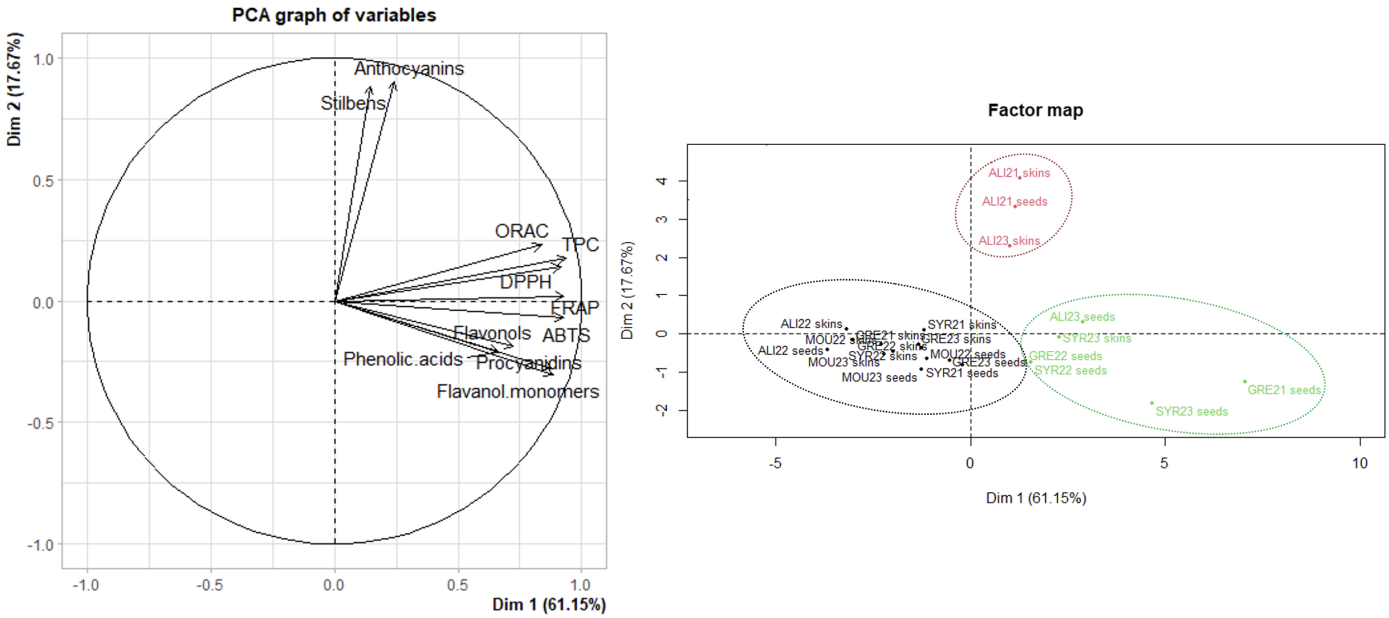


FIGURE 6. PCA plot.

A clear distinction was observed between seeds and skins, with seeds being richer in procyanidin dimers and flavanols, while skins exhibited higher anthocyanin content, as expected. Alicante skins exhibited the highest levels of anthocyanins and stilbenes, with elevated stilbene concentrations also observed in Alicante 2021 seeds, as previously described. Additionally, Grenache, Syrah, and Alicante seeds, along with Syrah skins, exhibited the highest antioxidant activity and flavan-3-ol content, showing consistent trends across vintages. These findings suggest that these grape varieties and their corresponding GP extracts may offer particularly promising candidates for applications targeting bioactive compounds.

Vintage-related differences were evident, with 2023 samples generally showing higher phenolic content and antioxidant activity, which may be attributed to climatic influences on polyphenol biosynthesis. Syrah and Alicante GP skins and seeds, as well as Grenache GP seeds, exhibited the highest phenolic levels and antioxidant capacities, while Mourvèdre consistently showed the lowest values, possibly due to greater degradation during vinification or inherent lower phenolic content. These results underscore the significant role of varietal differences in phenolic retention, with environmental factors such as temperature and ripening stage further influencing phenolic composition, as reflected in the observed vintage variations (Rienth *et al.*, 2021).

CONCLUSIONS

This study characterised the phenolic composition and antioxidant properties of grape pomace from red grape varieties cultivated in the Rhône Valley, France, emphasising their potential as a valuable by-product of winemaking. Despite partial extraction during vinification, GP extracts retained significant levels of flavan-3-ols, anthocyanins, and other bioactive phenolics. The distribution of these compounds varied across grape varieties and vintages, with seeds from Grenache, as well as skins and seeds from Syrah and Alicante, exhibiting the highest phenolic content and antioxidant capacity. These results identify these varieties as particularly promising for further exploration and valorisation

By investigating the relationships between phenolic composition and antioxidant activity, this research offers insights into the functional potential of GP and its suitability for future applications. The findings suggest that GP, especially from the identified high-potential varieties, offers a low-cost source of polyphenolic compounds that can be converted into bioactive extracts with diverse applications in the nutraceutical, cosmetic, and food industries. These extracts could serve as natural antioxidants in functional foods or as ingredients for enhancing product stability and shelf life. Future research should focus on optimising extraction and processing methods, refining antioxidant assessment techniques, and evaluating bioavailability to fully examine the potential of GP-derived compounds. This approach could enhance the economic and environmental value of GP, further establishing it as a key resource for sustainable utilisation within the winemaking industry.

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