

Saperavi wine by-products: a promising source of bioactive compounds

Khatuna Diasamidze, MD, PhD Candidate^{1,2*}, Maia Vanidze, PhD¹, Aleko Kalandia, PhD¹, Indira Jafaridze, PhD¹

¹ Department of Chemistry, Faculty of Natural Sciences and Health Care, Batumi Shota Rustaveli State University, Batumi, Georgia

² Medical Faculty, BAU International University Batumi, Batumi, Georgia

Abstract

Background Oxidative stress and chronic inflammation are central to the pathogenesis of cardiovascular and neurodegenerative disorders, which remain among the leading causes of mortality worldwide. Grape-derived polyphenols have attracted considerable interest because of their antioxidant, anti-inflammatory, and organoprotective properties.

Objective To investigate the phenolic composition and antioxidant potential of Saperavi winemaking by-products obtained in the Kakheti region during the 2024 harvest season, comparing unfermented and fermented grape skins and grape seeds.

Methods Saperavi grape skins and seeds (unfermented and fermented residues) were extracted by maceration in 75% ethanol. Total phenols were determined by the Folin–Ciocalteu method (chlorogenic acid equivalents); flavonoids by the AlCl₃ spectrophotometric method (quercetin equivalents); catechins by the vanillin assay ((+)-catechin equivalents); and leucoanthocyanins by the cyanidin-3-O-glucoside calibration. Antioxidant activity was assessed by the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assay at 517 nm.

Results Unfermented materials retained substantially higher concentrations of bioactive compounds than fermented residues. Unfermented grape seeds exhibited the highest total phenolic (207.89 mg/g) and flavonoid (162.48 mg/g) contents. In skins, total phenols decreased from 104.83 to 47.76 mg/g and leucoanthocyanins from 46.91 to 11.47 mg/g after fermentation. Unfermented grape skins displayed the strongest DPPH radical-scavenging activity, consistent with their elevated flavonoid and leucoanthocyanin content.

Conclusion Saperavi winemaking residues, particularly unfermented skins and seeds, represent promising raw materials for the recovery of natural antioxidant compounds. The findings support the sustainable valorization of Georgian winemaking by-products as candidate ingredients for nutraceutical, functional food, and related bioactive formulations within a circular bioeconomy framework.

Keywords Saperavi; *Vitis vinifera*; antioxidant activity; by-products; grape skin; grape seeds; polyphenols; nutraceuticals; circular bioeconomy

*Correspondence: khatuna.diasamidze16@bsu.edu.ge | ORCID: 0009-0009-6085-1695

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1. Introduction

Interest in biologically active compounds derived from plant materials has expanded markedly in recent decades because of their applications in the food, pharmaceutical, and nutraceutical industries. Among these compounds, polyphenols constitute one of the

most intensively studied classes of plant secondary metabolites owing to their antioxidant, anti-inflammatory, and cardioprotective properties [1,6,17,25].

Grapes (*Vitis vinifera* L.) are among the most economically important fruit crops worldwide, and

wine production generates large quantities of by-products, including grape skins and seeds. These residues typically account for approximately 20–30% of the original grape mass and still contain substantial amounts of biologically active compounds. Consequently, winemaking by-products are increasingly regarded as valuable raw materials rather than waste [7,8,9,11].

Polyphenolic compounds contribute to plant defence, pigmentation, and stress tolerance, while also influencing the sensory and functional properties of grapes and wine. Their redox-active chemical structure enables them to scavenge reactive oxygen species, chelate pro-oxidant metals, and modulate pathways associated with oxidative stress and inflammation. Through these mechanisms, polyphenols may help reduce processes linked with cardiovascular dysfunction, metabolic imbalance, and age-related degenerative conditions [12,24].

The distribution of phenolic compounds in grape tissues is not uniform. Leucoanthocyanins and flavonols are mainly concentrated in grape skins, whereas catechins and other flavan-3-ols are abundant in seeds and seed fractions [8,9,10]. Grape skins and seeds are therefore considered important reservoirs of bioactive compounds suitable for further recovery and valorisation [12,24].

The concept of a circular bioeconomy has stimulated interest in the reuse of agro-industrial residues as sustainable sources of high-value compounds. Grape by-products have therefore attracted increasing attention as candidate ingredients for natural antioxidant extracts, functional food formulations, and nutraceutical applications.

1.1 Antioxidant and anti-inflammatory mechanisms

The Keap1–Nrf2 signalling pathway represents the principal inducible defence mechanism against oxidative stress. Since the identification of Nrf2 as the transcription factor governing cytoprotective gene expression, an intricate molecular regulatory network has been elucidated in which the stress-sensor protein Keap1 exerts tight control over Nrf2 activity. Upon exposure to oxidative or electrophilic stress, Keap1-mediated ubiquitin-ligase activity is impaired, leading to Nrf2 stabilisation, nuclear translocation, and subsequent activation of antioxidant and anti-inflammatory gene programmes [1,5,6,20].

Polyphenols neutralise reactive oxygen species (ROS) by scavenging free radicals, inhibiting ROS-generating enzymes such as NADPH oxidase, xanthine oxidase, and lipoxygenase, and supporting endogenous antioxidant systems including catalase.

These actions limit lipid peroxidation—notably oxidation of low-density lipoprotein (LDL)—and protect endothelial cells from oxidative injury, both early steps in atherosclerotic plaque formation. Chelation of pro-oxidant metals such as iron further constrains Fenton-type reactions that amplify oxidative stress [2,5,6,16,20].

Polyphenols also down-regulate pro-inflammatory cytokines (TNF- α , IL-6) and signalling intermediates such as NF- κ B in cardiomyocytes and vascular tissues, attenuating the chronic inflammation that drives cardiovascular disease. Inhibition of cyclooxygenase (COX) pathways further reduces endothelium-derived contracting factors and supports vascular tone [4,18].

1.2 Endothelial, vascular, and lipid effects

Polyphenols enhance nitric-oxide (NO) bioavailability by upregulating endothelial NO synthase (eNOS), thereby promoting vasodilation and inhibiting platelet aggregation and adhesion. They improve endothelial function, contribute to blood-pressure control through angiotensin II modulation, and limit smooth-muscle-cell proliferation [2,15,22].

By reducing LDL oxidation and supporting high-density lipoprotein (HDL) function, polyphenols hinder foam-cell formation and atherosclerotic plaque accumulation. Their antithrombotic activity reflects suppressed platelet activation and reduced thrombus propagation [15,22].

The protective profile of red-wine polyphenols is consistent with the so-called "French paradox"—the observation of comparatively low cardiovascular mortality in populations consuming red wine alongside diets rich in saturated fat. Regular consumption of polyphenol-rich foods has been associated with reduced risks of cancer, cardiovascular disease, and age-related cognitive decline, including Alzheimer's disease [2,4,15,22]. Flavonoids in grape skins and seeds further demonstrate cytotoxic, anti-proliferative, and stress-protective effects in experimental models, and stems and skins likewise represent rich sources of phenolic compounds [19,20,21,22].

1.3 Saperavi and the Georgian context

Georgia is recognised as one of the oldest wine-producing regions in the world and is distinguished by a rich diversity of indigenous grape varieties. Among them, Saperavi is one of the most important red cultivars, widely cultivated in Eastern Georgia and especially in the Kakheti region. The variety is characterised by intense pigmentation and a high phenolic potential, which makes it particularly

attractive for the investigation of bioactive compounds in both grapes and winemaking residues [14].

Despite the long-standing importance of Georgian viticulture, the chemical characterisation and valorisation potential of Saperavi winemaking residues remain insufficiently explored. A clearer understanding of the composition of these by-products could support their use as sustainable sources of natural antioxidants and other functional ingredients.

1.4 Aim and objectives

The aim of the present study was to investigate the phenolic composition and antioxidant potential of Saperavi grape skins and grape seeds obtained in the Kakheti region during the 2024 harvest season. Special attention was given to comparing unfermented and fermented residues in order to assess how the winemaking process affects retention of phenolic compounds in the residual solid fractions.

The specific objectives were: (i) to quantify total phenols, flavonoids, catechins, and leucoanthocyanins in unfermented and fermented Saperavi grape skins and seeds; (ii) to compare the phenolic retention of residues before and after fermentation; (iii) to assess antioxidant activity by the DPPH radical-scavenging assay; and (iv) to discuss the potential of these materials as sustainable sources of value-added bioactive compounds.

2. Materials and methods

2.1 Materials

Saperavi grape skins and seeds were collected from the Kakheti region of Eastern Georgia during the 2024 harvest season. Both unfermented (fresh winery residues recovered immediately after pressing) and fermented (residues recovered after completion of red-wine maceration and fermentation) materials were used as analytical samples. Samples were kept refrigerated and processed under standardised laboratory conditions.

2.2 Extraction

All samples (skins and seeds) were subjected to maceration with 75% (v/v) ethanol prior to analytical determination. Extracts were filtered and stored protected from light at 4 °C until measurement.

2.3 Total phenolic content

Total phenols were determined by the Folin–Ciocalteu method [12,13,14,23,24]. Briefly, 1 mL of Folin–Ciocalteu reagent was added to 1 mL of extract; after 3 min, 1 mL of 10% Na₂CO₃ was added and the volume was brought to 10 mL with distilled

water. After 90 min of incubation, optical density was measured at 750 nm. Results were expressed as chlorogenic-acid equivalents (mg/g sample).

2.4 Total flavonoid content

Total flavonoids were determined by the AlCl₃ spectrophotometric method [12,13,14,23,24]. A 1 mL aliquot of extract was transferred to a 10 mL test tube; 5 mL water and 0.3 mL of 5% NaNO₂ were added and incubated for 5 min, then 0.3 mL of 10% AlCl₃ was added and incubated for a further 6 min. Finally, 2 mL of 1 N NaOH was added and absorbance was measured at 510 nm. Results were expressed as quercetin equivalents (mg/g sample).

2.5 Total catechin content

Total catechins were determined by the vanillin assay [12,13,14,23,24]. A 1 mL aliquot of extract was mixed with 3 mL of vanillin reagent; after 3 min the optical density of the resulting red solution was measured at 500 nm. A control containing the same reagents without extract was prepared in parallel. Catechin concentration was determined from a (+)-catechin calibration curve, and results were expressed as mg catechin equivalents per gram of sample.

2.6 Leucoanthocyanin content

Leucoanthocyanins were quantified using a bisulphite-converted heating procedure [12,13,14,24]. To 1 mL of extract, 8 mL of leucoanthocyanidin reagent was added; for each sample a parallel unheated control was prepared. The test sample was heated for 40 min, after which both samples were measured at 550 nm, with the unheated sample serving as the control. Results were converted to mg/g dry weight using a cyanidin-3-O-glucoside calibration curve.

2.7 Antioxidant activity

Antioxidant activity was evaluated using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical-scavenging assay [3,13,24]. A 1.0 mL aliquot of extract was mixed with 3.0 mL of 0.1 mM DPPH methanolic solution and incubated in the dark at room temperature for 15 min. Absorbance was measured at 517 nm. Percentage inhibition of DPPH radicals was calculated from the absorbance of control and sample mixtures, and the extract concentration required to achieve 50% inhibition (IC₅₀) was determined by interpolation.

2.8 Data presentation

Quantitative results for each phenolic class are summarised in Table 1; phenolic profiles of skins and seeds are visualised in Figure 1 and Figure 2 respectively. Given the exploratory, single-harvest

sampling design, results are reported as point estimates; replicate-based statistical analysis is identified as a priority for future work (see Discussion).

Table 1. Phenolic composition of Saperavi winemaking by-products from the Kakheti region (2024 harvest), expressed in mg per g of dry weight. n.r. = not reported in the source dataset.

Phenolic group	Unfermented skins	Fermented skins	Unfermented seeds	Fermented seeds
Total phenols	104.83	47.76	207.89	n.r.
Flavonoids	101.67	34.82	162.48	n.r.
Catechins	12.37	9.65	18.07	n.r.
Leucoanthocyanins	46.91	11.47	45.32	n.r.

3. Results

3.1 Phenolic composition of grape skins

In grape skins, total phenols decreased from 104.83 mg/g in unfermented material to 47.76 mg/g after fermentation. Flavonoids showed a similar decline,

from 101.67 to 34.82 mg/g, while catechins decreased modestly from 12.37 to 9.65 mg/g. Leucoanthocyanins exhibited the most pronounced reduction, falling from 46.91 to 11.47 mg/g (Figure 1; Table 1). This pattern is consistent with the known extractability of skin-derived pigments and flavonoids during red winemaking.

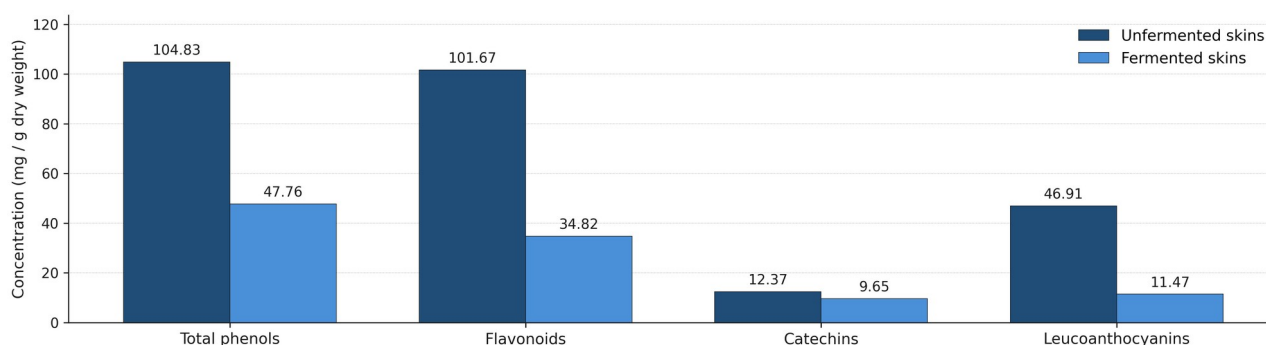


Figure 1. Phenolic composition of Saperavi grape skins, unfermented and fermented residues, from the Kakheti region (2024 harvest). Concentrations are expressed as mg per g of dry weight.

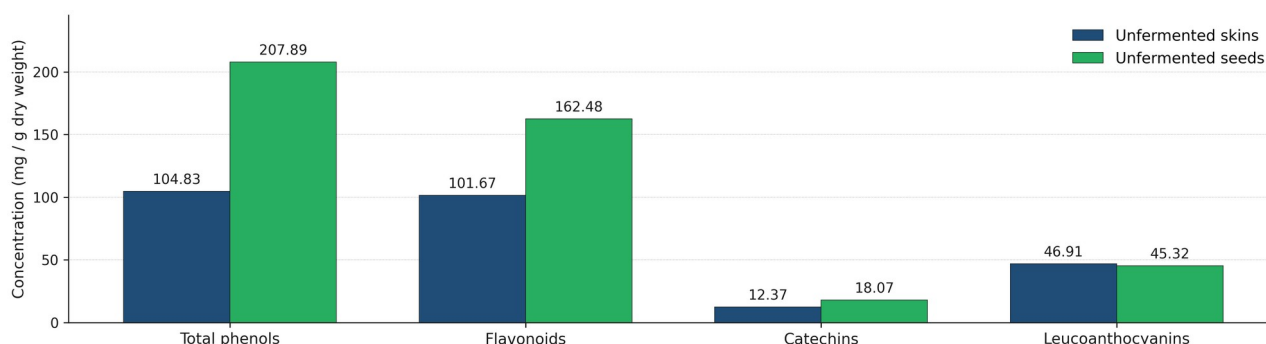


Figure 2. Comparative phenolic composition of unfermented Saperavi grape skins and unfermented grape seeds from the Kakheti region (2024 harvest). Concentrations are expressed as mg per g of dry weight.

3.2 Phenolic composition of grape seeds

In grape seeds, unfermented samples showed the highest overall concentrations among all analysed residues, with 207.89 mg/g total phenols, 162.48 mg/g flavonoids, 18.07 mg/g catechins, and 45.32 mg/g leucoanthocyanins (Table 1; Figure 2). These values indicate that freshly recovered seeds represent a particularly rich source of polyphenolic compounds. After fermentation, all measured groups declined substantially, again confirming the redistribution of phenolics from the solid matrix into the liquid phase during processing; quantitative values for the fermented seed fraction were not separately reported in the source dataset.

3.3 Antioxidant activity

DPPH-based antioxidant evaluation supported the compositional findings. Unfermented grape skins showed the most pronounced antioxidant performance, consistent with their elevated flavonoid and leucoanthocyanin contents. In phenolic-rich plant matrices, radical-scavenging activity is commonly associated with the capacity of these compounds to donate electrons or hydrogen atoms and to stabilise reactive intermediates. Unfermented seeds, despite their high total phenolic and flavonoid content, exhibited a slightly lower DPPH-scavenging response, suggesting that the qualitative profile of the polyphenolic mixture—and not solely its total mass—governs antioxidant activity.

4. Discussion

4.1 Phenolic redistribution during fermentation

The marked decrease of total phenols, flavonoids, and leucoanthocyanins in fermented skins is consistent with the well-described extraction dynamics of red winemaking, in which alcohol-driven maceration progressively transfers anthocyanins, tannins, and flavonols from skin tissue into the must [6,8,11]. The pronounced reduction of leucoanthocyanins in particular reflects the central role of these pigments in the development of red-wine colour. The persistence of measurable phenolic concentrations in fermented residues nonetheless indicates that the by-product retains an appreciable bioactive fraction with potential technological value.

4.2 Seeds as a concentrated polyphenol reservoir

The high retention of phenolic compounds in unfermented seeds is particularly relevant from a valorisation perspective. Grape seeds are well

established as concentrated sources of flavan-3-ols (catechins, epicatechins) and proanthocyanidins [4,7,11,17], and the present results extend this evidence base to Saperavi residues. The differential between unfermented seed (≈ 208 mg/g total phenols) and unfermented skin (≈ 105 mg/g) values approximates a two-fold concentration advantage, which is in agreement with previously reported skin-vs-seed ratios for red *Vitis vinifera* cultivars [4,21]. Practical recovery of seed-derived polyphenols from winery residues therefore appears to offer an efficient pathway for ingredient development.

4.3 Antioxidant performance and structure–activity considerations

The observation that unfermented skins outperformed unfermented seeds in the DPPH assay—despite seeds having higher total polyphenol mass—mirrors observations reported for several *Vitis* varieties, where the qualitative phenolic profile (notably anthocyanin and flavonol content) often drives radical-scavenging activity more than total polyphenol mass alone [9,16,19,20]. The high leucoanthocyanin and flavonoid content of skins is consistent with this interpretation. Future work using HPLC- and UPLC-MS profiling, including procyanidin oligomer characterisation, would clarify the chemical drivers of antioxidant activity in Saperavi residues [23].

4.4 Implications for nutraceutical and functional-food applications

The compositional and antioxidant findings support the use of Saperavi by-products as candidate raw materials for natural antioxidant extracts. Polyphenol-enriched extracts from grape residues have been investigated as functional ingredients in beverages, dairy and bakery products, and in formulations targeting cardiovascular and metabolic risk factors [2,15,18,22]. The bioavailability and stability of polyphenols can additionally be improved through encapsulation strategies, with growing evidence from grape-seed phenolic systems supporting industrial feasibility [16,17]. Within a circular bioeconomy framework, valorisation of these residues could increase the added value of Georgian viticultural production while reducing agro-industrial waste streams [12,13,23].

4.5 Limitations

Several limitations should be acknowledged. The present analysis is based on a single harvest year and a single regional source (Kakheti, 2024); inter-annual and microclimatic variability are known to affect grape-residue polyphenol profiles and warrant

systematic study. Quantitative values for the fermented seed fraction were not separately reported, limiting comparison of fermentation-related changes between matrices. Replicate-based descriptive statistics are not provided in the source dataset and are identified as a priority for follow-up work, together with HPLC- and UPLC-MS chromatographic profiling, in vitro bioavailability assessment, and bioactivity-guided fractionation.

5. Conclusion

The present study demonstrates that Saperavi winemaking by-products retain substantial concentrations of phenolic compounds and represent promising raw materials for the recovery of natural bioactive ingredients. Among the examined matrices, unfermented grape seeds showed the highest concentrations of total phenols, flavonoids, and catechins, whereas unfermented grape skins displayed the most pronounced antioxidant potential. Fermented residues contained markedly lower concentrations of these compounds, confirming substantial transfer of phenolics into the wine matrix during fermentation.

Overall, the findings support the sustainable valorisation of Saperavi by-products as raw materials for the development of antioxidant-rich extracts and related value-added applications. Such products may contribute as adjunctive nutritional strategies to the prevention and management of cardiovascular and neurodegenerative conditions whose pathogenesis involves oxidative stress and chronic inflammation. Further work integrating replicate-based statistics, expanded chromatographic profiling, and bioactivity-guided validation will be required to define the practical nutraceutical and functional-food potential of these materials.

Abbreviations

AlCl₃ — Aluminium chloride
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CI — Confidence Interval
COX — Cyclo-oxygenase
CVD — Cardiovascular disease
DOI — Digital Object Identifier
DPPH — 2,2-Diphenyl-1-picrylhydrazyl
eNOS — Endothelial nitric oxide synthase
GMJ — Georgian Medical Journal
HDL — High-density lipoprotein
HPLC — High-performance liquid chromatography
IC₅₀ — Concentration providing 50% inhibition
IL-6 — Interleukin-6
Keap1 — Kelch-like ECH-associated protein 1

LDL — Low-density lipoprotein
NF-κB — Nuclear factor kappa-light-chain-enhancer of activated B cells
NO — Nitric oxide
Nrf2 — Nuclear factor erythroid 2-related factor 2
ORCID — Open Researcher and Contributor ID
PHIG — Public Health Institute of Georgia
ROS — Reactive oxygen species
TNF-α — Tumour necrosis factor alpha
UPLC-MS — Ultra-performance liquid chromatography–mass spectrometry

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Authors' contributions

KhD: Conceptualisation; investigation; methodology; data curation; formal analysis; writing — original draft; final approval. MV: Conceptualisation; methodology; supervision; validation; writing — review and editing; final approval. AK: Methodology; validation; resources; writing — review and editing; final approval. IJ: Investigation; data curation; validation; final approval. All authors read and approved the final manuscript.

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Declarations

Ethics approval and consent to participate Not applicable. The study did not involve human participants, identifiable personal information, or animal subjects; all analyses were performed on plant-derived winemaking by-products.

Consent for publication Not applicable. The article does not contain any individual-level or identifying personal information.

Conflict of interest disclosures The authors declare no competing interests, financial or non-financial, related to the subject matter of this article.

Data sharing All quantitative data underlying the present analysis are reported in full in Table 1 and Figures 1–2 of this article. The article is archived under its DOI (10.66636/gmj.v1.i2.a121) and deposited via the journal's preservation infrastructure (Zenodo, PKP PN, LOCKSS, DataCite). Additional raw spectrophotometric records are available from the corresponding author on reasonable request.

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Author details

¹ Department of Chemistry, Faculty of Natural Sciences and Health Care, Batumi Shota Rustaveli State University, Batumi, Georgia.

² Medical Faculty, BAU International University Batumi, Batumi, Georgia.

ORCID iDs.

Khatuna Diasamidze: <https://orcid.org/0009-0009-6085-1695>

Maia Vanidze: <https://orcid.org/0000-0003-0807-0735>

Aleko Kalandia: <https://orcid.org/0000-0001-9570-9263>

Indira Jafaridze: <https://orcid.org/0000-0003-2088-212X>

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