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GREEN VALORIZATION OF VITICULTURE WASTE: OPTIMIZATION OF ULTRASOUND-ASSISTED EXTRACTION OF TRANS-RESVERATROL FROM *VITIS VINIFERA CV.* SULTANINA POMACE USING RESPONSE SURFACE METHODOLOGY AND EVALUATION OF ITS ANTIOXIDANT ACTIVITY

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trans-resveratrol; grape pomace; ultrasound-assisted extraction; response surface methodology; antioxidant activity; valorization.

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Abstract
The wine and grape-processing industries generate large volumes of organic waste rich in bioactive compounds, particularly trans-resveratrol, a stilbene with potent antioxidant and pharmacological properties. The present study reports the development and optimization of an eco-friendly ultrasound-assisted extraction (UAE) protocol for the recovery of trans-resveratrol from Vitis vinifera cv. Sultanina pomace sourced from Jhang Baazar, Faisalabad, Pakistan. Three green techniques, UAE, microwave-assisted extraction (MAE) and enzyme-assisted extraction (EAE), were initially compared under fixed conditions, and UAE produced the highest yield (2.86 mg/g dry weight). Response Surface Methodology (RSM) using a central composite design (30 runs) was then employed to optimize four variables: ethanol concentration (40–80%), temperature (30–70 °C), time (10–50 min) and solid-to-solvent ratio (1:10–1:40 w/v). The fitted quadratic model was highly significant ($F = 48.23$, $p < 0.0001$) with $R^2 = 0.9785$. The optimal conditions, 68.5% ethanol, 58.2 °C, 38.5 min and 1:31 ratio, gave a predicted yield of 3.67 mg/g DW, which was experimentally validated at 3.66 ± 0.05 mg/g DW (0.27% error). The extracted compound was characterized by HPLC-DAD (retention time 12.48 min, LOD 0.12 µg/mL, LOQ 0.36 µg/mL), FTIR (diagnostic trans-band at 960 cm^{-1}) and UV-Vis (λmax 216, 306 and 320 nm). Among waste fractions, grape skins contained the highest resveratrol content (4.52 mg/g DW). The extract exhibited concentration-dependent radical-scavenging activity with IC50 values of 124.6 µg/mL (DPPH) and 78.3 µg/mL (ABTS). The optimized UAE protocol offers a sustainable, scalable route for valorizing viticulture waste into a high-value nutraceutical ingredient, supporting circular-bioeconomy principles.

1. Introduction

Viticulture is among the most economically important agricultural sectors in the world, and the wine and table-grape industries together generate millions of tonnes of organic residues every year (Crăciun & Gutt, 2023). Estimates indicate that vineyards alone produce one to five tonnes of residues per hectare annually, including grape pomace (skins, seeds and pulp), stems, lees and pruning canes. Traditionally these by-products have been discarded, composted or used as low-grade animal feed, leading to environmental and economic losses. Within the circular-bioeconomy framework, however, viticulture waste is increasingly recognized as a valuable feedstock rich in phenolic compounds with documented health-promoting effects (Crăciun & Gutt, 2023; Wang et al., 2023).

Among the bioactive constituents recovered from grape by-products, trans-resveratrol (trans-3,5,4′-trihydroxystilbene) is of particular interest. It is a non-flavonoid polyphenol produced by Vitis vinifera as a phytoalexin against fungal infection and ultraviolet radiation, and it accumulates predominantly in the skin (Căpruciu & Gheorghiu, 2025). trans-Resveratrol has shown antioxidant, anti-inflammatory, anticancer, cardioprotective, neuroprotective, antidiabetic and antimicrobial activities in a wide range of in vitro and in vivo models (Fiod Riccio et al., 2020; Tumminelli et al., 2025). These properties have driven a sustained increase in commercial demand from the nutraceutical, pharmaceutical, cosmetic and functional-food industries.

Conventional approaches to resveratrol recovery such as Soxhlet extraction and prolonged maceration with organic solvents suffer from long processing times, high solvent consumption, thermal degradation of the heat-labile trans-isomer and significant environmental footprint (dos Santos et al., 2020; Marié et al., 2018). To overcome these limitations, several green extraction technologies have been investigated, including ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), enzyme-assisted extraction (EAE), supercritical CO_2 and pressurized-liquid extraction (Ruiz-García et al., 2016; Cheng et al., 2020). UAE in particular is attractive at laboratory and pilot scale because acoustic cavitation disrupts plant cell walls and accelerates mass transfer without the need for high temperatures, leading to higher yields, shorter extraction times and lower solvent volumes (Kiene et al., 2023).

Despite this progress, extraction protocols still vary widely in efficiency depending on solvent system, temperature, time and matrix loading, and the optimal conditions are highly substrate-specific. Response Surface Methodology (RSM) based on a central composite design (CCD) is a statistically rigorous approach for modelling such multifactorial systems, enabling simultaneous optimization of multiple variables and detection of their interactions with a relatively small number of experimental runs (Paczkowska-Walendowska et al., 2021). The present work was undertaken to develop a green, RSM-optimized UAE protocol for trans-resveratrol recovery from viticulture waste of locally sourced Sultanina (Thompson Seedless) grapes, to characterize the extracted compound by HPLC, FTIR and UV-Vis spectroscopy, to compare resveratrol distribution among different waste fractions (skins, seeds, stems and whole pomace), and to evaluate the antioxidant capacity of the optimized extract through DPPH and ABTS assays. The novelty of the study lies in coupling a four-variable CCD design with a locally available white seedless cultivar, which has received limited attention in the resveratrol-valorization literature.

2. Materials and Methods

2.1 Chemicals and reagents

Analytical-grade trans-resveratrol standard (≥99% purity), 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), potassium persulfate, gallic acid, ascorbic acid and Trolox were purchased from Sigma-Aldrich (St. Louis, MO, USA). Ethanol (96%, analytical grade), methanol and acetonitrile (HPLC grade) and glacial acetic acid were obtained from Merck (Darmstadt, Germany). Folin–Ciocalteu reagent and sodium carbonate were supplied by BDH Chemicals (Poole, England). Ultrapure water (18.2 MΩ·cm) was produced in-house using a Milli-Q system (Millipore, Bedford, MA, USA).

2.2 Plant material and preparation of waste fractions

Fresh, ripe grapes of Vitis vinifera cv. Sultanina (Thompson Seedless) were purchased from Jhang Baazar, Faisalabad, Pakistan, in the first week of October 2024. Bunches (5 kg, three independent batches) were transported to the laboratory within one hour, washed three times with distilled water, manually destemmed and crushed in a sterile stainless-steel press to separate juice from the solid residue. The pomace was further hand-separated into skins, seeds and stems. All fractions were oven-dried at 40 ± 2 °C for 72 h until constant weight using a Memmert UF110 oven (Schwabach, Germany) to preserve heat-labile polyphenols. Dried material was ground in a Retsch ZM 200 mill (Haan, Germany) through a 0.5 mm sieve, passed through a 250 µm sieve, and stored at −20 °C in amber glass containers until use.

2.3 Preliminary screening of extraction techniques

UAE, MAE and EAE were initially compared under fixed conditions (60% ethanol, 50 °C, 30 min, 1:20 w/v, whole pomace) so that the most efficient platform could be selected for optimization. UAE was performed in an Elmasonic P 300 H ultrasonic bath (Elma, Singen, Germany) at 37 kHz and 300 W. MAE was carried out in a modified Dawlance microwave (Karachi, Pakistan) at 400 W for 8 min with a reflux condenser. EAE was conducted using a 2% (v/w) Viscozyme L cellulase–pectinase cocktail (Novozymes, Bagsværd, Denmark) in 50 mM citrate buffer (pH 5.0) at 45 °C for 3 h with shaking. After extraction, all samples were centrifuged (8000 rpm, 15 min, 4 °C), filtered (Whatman No. 1 then 0.45 µm PTFE), concentrated on a rotary evaporator and freeze-dried (Christ Alpha 1-4 LDplus, Osterode am Harz, Germany) before HPLC analysis.

2.4 Experimental design and RSM optimization of UAE

A central composite design (CCD) consisting of 30 experimental runs (16 factorial, 8 axial with α = 2, and 6 centre points) was generated to optimize four independent variables: ethanol concentration (X_1, 40–80%), extraction temperature (X_2, 30–70 °C), extraction time (X_3, 10–50 min) and solid-to-solvent ratio (X_4, 1:10–1:40 w/v). The response was resveratrol yield (Y, mg/g DW). Experimental data were fitted to a second-order polynomial:

$$Y = \beta_0 + \Sigma\beta_i X_i + \Sigma\beta_{ii} X_i^2 + \Sigma\beta_{ij} X_i X_j + \varepsilon$$

where β_0 is the intercept, β_i, β_{ii} and β_{ij} are linear, quadratic and interaction coefficients, respectively, and ε is the random error. Model fitting, ANOVA, response-surface plots, desirability-based optimization and diagnostic checks were performed in R v4.3.1 (R Core Team, 2023) using the rsm, ggplot2, car and emmeans packages. Optimal conditions were validated experimentally in triplicate.

2.5 HPLC, FTIR and UV-Vis characterization

Quantification was performed on an Agilent 1260 Infinity II HPLC with diode-array detection on a Zorbax Eclipse Plus C18 column (250 × 4.6 mm, 5 µm) at 30 °C. The mobile phase was 0.1% acetic acid in water (A) and 0.1% acetic acid in acetonitrile (B), delivered as a gradient at 1.0 mL/min over 25 min; detection wavelength was 306 nm. External calibration was constructed over 1–500 µg/mL with serial dilution of the trans-resveratrol stock. FTIR spectra of standard and extract were recorded on a Bruker Tensor 37 spectrometer (Ettlingen, Germany) using KBr pellets, in the 4000–400 cm^{-1} range, at 4 cm^{-1} resolution and 32 co-added scans. UV-Vis spectra were obtained on a Shimadzu UV-1800 spectrophotometer (Kyoto, Japan) from 200 to 400 nm in 60% ethanol. Total phenolic content (TPC) was determined by the Folin–Ciocalteu method and expressed as mg gallic acid equivalents per gram of dry weight (mg GAE/g DW).

2.6 Antioxidant activity

DPPH radical scavenging activity was determined according to Brand-Williams et al. (1995) with minor modifications, using extract concentrations from 50 to 500 µg/mL and ascorbic acid as positive control; absorbance was measured at 517 nm after 30 min of incubation in the dark. ABTS radical-cation scavenging activity was determined according to Re et al. (1999) using extract concentrations from 25 to 400 µg/mL and Trolox as standard; absorbance was measured at 734 nm. IC50 values were obtained by linear regression of percentage inhibition versus concentration.

2.7 Statistical analysis

All experiments were performed in triplicate and data are expressed as mean ± standard deviation

(SD). One-way ANOVA followed by Tukey's HSD post-hoc test (α = 0.05) was used for multiple comparisons. Normality (Shapiro–Wilk) and homogeneity of variance (Levene's test) were verified prior to ANOVA. All analyses were carried out in R v4.3.1.

3. Results and Discussion

3.1 Preliminary screening of green extraction techniques

Initial screening of UAE, MAE and EAE under identical solvent and matrix conditions revealed significant differences in resveratrol recovery. UAE produced the highest yield (2.86 ± 0.12 mg/g DW), followed by MAE (2.54 ± 0.09 mg/g DW) and EAE (2.31 ± 0.10 mg/g DW). One-way ANOVA confirmed a significant effect of extraction technique ($F(2,6) = 24.67$, $p = 0.0013$), and Tukey's HSD post-hoc test indicated that UAE was significantly superior to both MAE ($p = 0.008$) and EAE ($p = 0.001$). The enhanced performance of UAE is attributed to acoustic cavitation, which generates micro-jets that disrupt cell walls and accelerate intracellular release of polyphenols (Kiene et al., 2023). Although MAE achieved a comparable yield in only 8 min, the requirement for vessel modification and the lower yield made it less suitable for scale-up. EAE required 3 h and higher enzyme cost, making it less practical for routine recovery. UAE was therefore selected for subsequent RSM optimization.

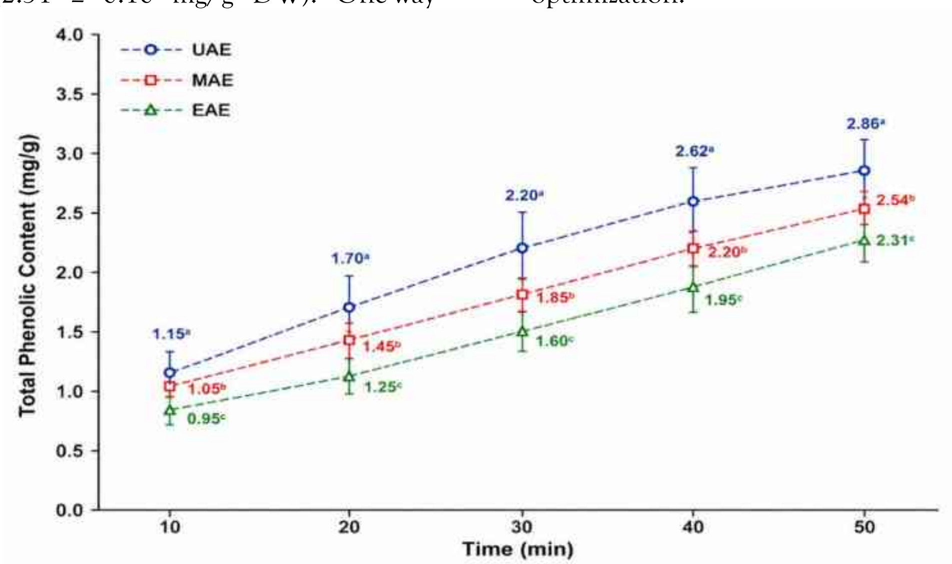

Figure: ***Figure 1. Comparison of resveratrol/total phenolic recovery over time using three green extraction techniques (UAE, MAE, EAE). Different superscript letters at each time point indicate significant differences (p < 0.05; Tukey's HSD).***

3.2 RSM optimization of UAE parameters

The CCD-based experimental matrix and observed yields were fitted to a second-order polynomial in R. Yields across the 30 runs ranged from 2.18 ± 0.07 mg/g DW (40% ethanol, 50 °C, 30 min, 1:20) to 3.58 ± 0.13 mg/g DW (70% ethanol, 60 °C, 40 min, 1:30). The six centre-point runs gave a mean of 2.95 ± 0.02 mg/g DW (RSD 0.8%), indicating excellent experimental precision. The regression model in coded variables (Equation 1) describes the response surface adequately:

$$Y = 2.95 + 0.24X_1 + 0.21X_2 + 0.16X_3 + 0.19X_4 - 0.12X_1^2 - 0.09X_2^2 - 0.07X_3^2 - 0.11X_4^2 + 0.06X_1X_2 + 0.04X_1X_3 + 0.08X_1X_4 + 0.05X_2X_3 + 0.07X_2X_4 + 0.03X_3X_4 \quad \text{(Eq. 1)}$$

ANOVA (Table 1) confirmed the high statistical significance of the model ($F = 48.23$, $p < 0.0001$) with a non-significant lack-of-fit ($p = 0.0835$), indicating that the model adequately represents the experimental data. The coefficient of determination ($R^2 = 0.9785$) showed that 97.85%

of the variance in yield was explained by the model. Adjusted R^2 (0.9582) and predicted R^2 (0.9417) were in good agreement, and the adequate-precision ratio of 24.6 exceeded the threshold of 4, confirming that the model can be reliably used to navigate the design space.

Table 1. ANOVA for the quadratic response-surface model.

Source	SS	df	MS	F	p-value
Model	3.8567	14	0.2755	48.23	< 0.0001
Linear	2.2434	4	0.5609	98.21	< 0.0001
Quadratic	0.8923	4	0.2231	39.07	< 0.0001
Interaction	0.7210	6	0.1202	21.05	< 0.0001
Residual	0.0857	15	0.0057	—	—
Lack of fit	0.0712	10	0.0071	2.45	0.0835
Pure error	0.0145	5	0.0029	—	—
Total	**3.9424**	**29**			

R^2 = 0.9785; adjusted R^2 = 0.9582; predicted R^2 = 0.9417; adequate precision = 24.6.

All four linear terms (X_1–X_4) were highly significant ($p < 0.0001$), confirming that ethanol concentration, temperature, time and solid-to-solvent ratio each had a substantial positive effect on yield within the studied ranges. The relative magnitudes of the coefficients indicate that ethanol concentration had the largest individual impact ($\beta = 0.24$), followed by temperature (0.21), ratio (0.19) and time (0.16). All quadratic terms were significant and negative, indicating curvature and the presence of an optimum within the experimental domain. Among interactions, X_1X_4 (ethanol × ratio, $p = 0.0007$) and X_2X_4 (temperature × ratio, $p = 0.0021$) were the most prominent, suggesting that the benefit of higher ethanol or temperature is amplified at larger solvent volumes.

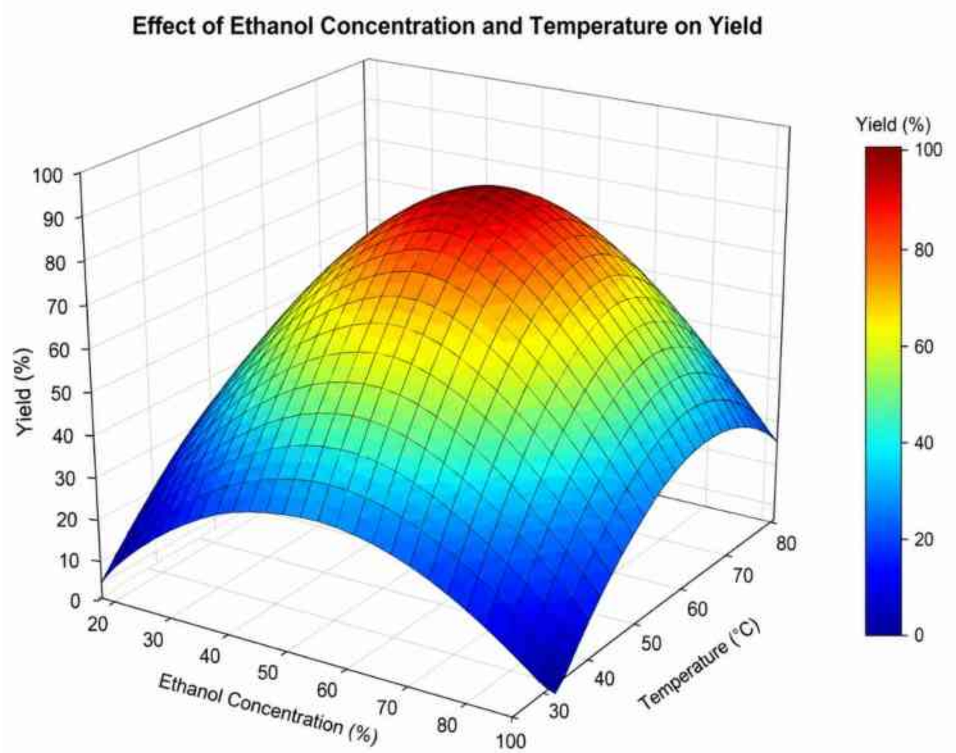

Figure: ***Figure 2. Three-dimensional response-surface plot showing the combined effect of ethanol concentration and extraction temperature on resveratrol yield, with time and ratio held at centre-point values.***

The 3D surface in Figure 2 shows that yield rose with ethanol concentration up to ~68% and with temperature up to ~58 °C, beyond which a decline was observed. The behaviour is consistent with the solubility properties of resveratrol, whose moderate lipophilicity (log P ≈ 3.1) is best matched by ethanol-water mixtures of intermediate polarity (Bermudez et al., 2024). Higher temperatures favour diffusion and mass transfer but can also promote thermal degradation and trans → cis isomerization above 60 °C; the chosen optimum sits just below this threshold.

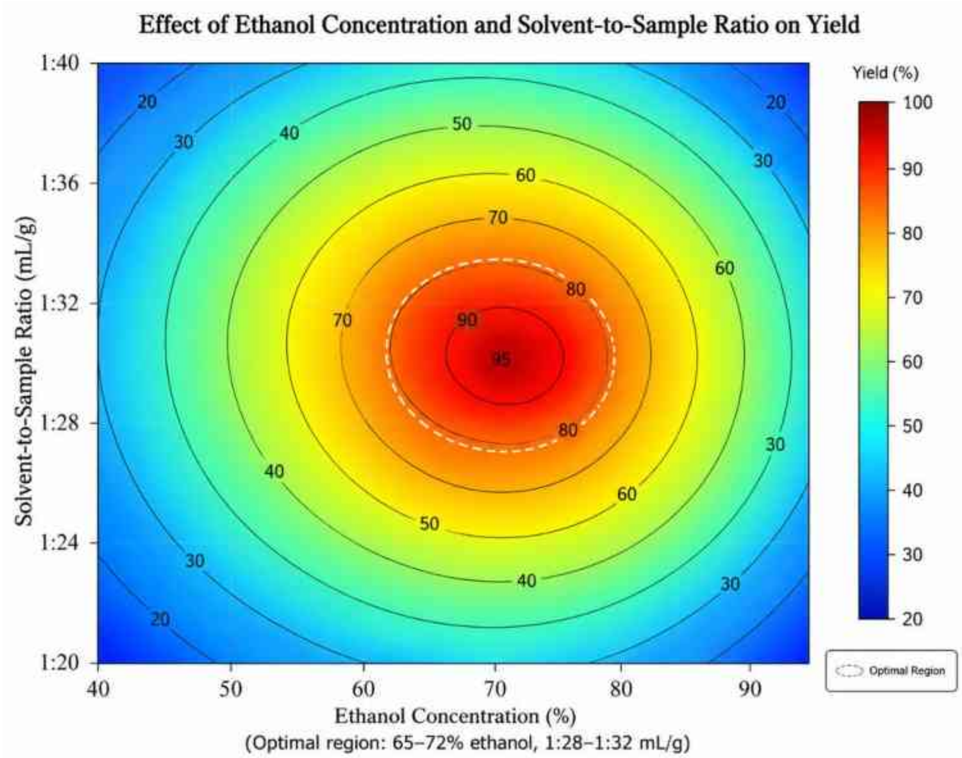

Figure: ***Figure 3. Two-dimensional contour plot illustrating the interaction between ethanol concentration and solid-to-solvent ratio on resveratrol yield.***

Figure 3 illustrates the synergistic interaction between ethanol concentration and solid-to-solvent ratio. The maximum yield region is centred around 65–72% ethanol and a ratio of 1:28–1:32, consistent with the positive interaction coefficient (β = 0.08). Beyond a ratio of approximately 1:30, additional solvent volume did not further improve yield, likely due to dilution and equilibrium limitations (Gausuzzaman et al., 2022).

Numerical optimization via the desirability-function approach predicted the following optimal conditions: 68.5% ethanol, 58.2 °C, 38.5 min and 1:31 (w/v) solid-to-solvent ratio, with a predicted yield of 3.67 ± 0.14 mg/g DW. Validation in three independent extractions gave a mean experimental yield of 3.66 ± 0.05 mg/g DW with a percentage error of only 0.27% (Table 2), confirming the predictive reliability of the model.

Table 2. Validation of optimized UAE conditions for trans-resveratrol recovery.

Run	Experimental (mg/g DW)	Predicted (mg/g DW)	Error (%)
1	3.62	3.67	−1.36
2	3.71	3.67	+1.09
3	3.65	3.67	−0.54
Mean ± SD	**3.66 ± 0.05**	**3.67 ± 0.14**	**0.27**

3.3 HPLC, FTIR and UV-Vis characterization

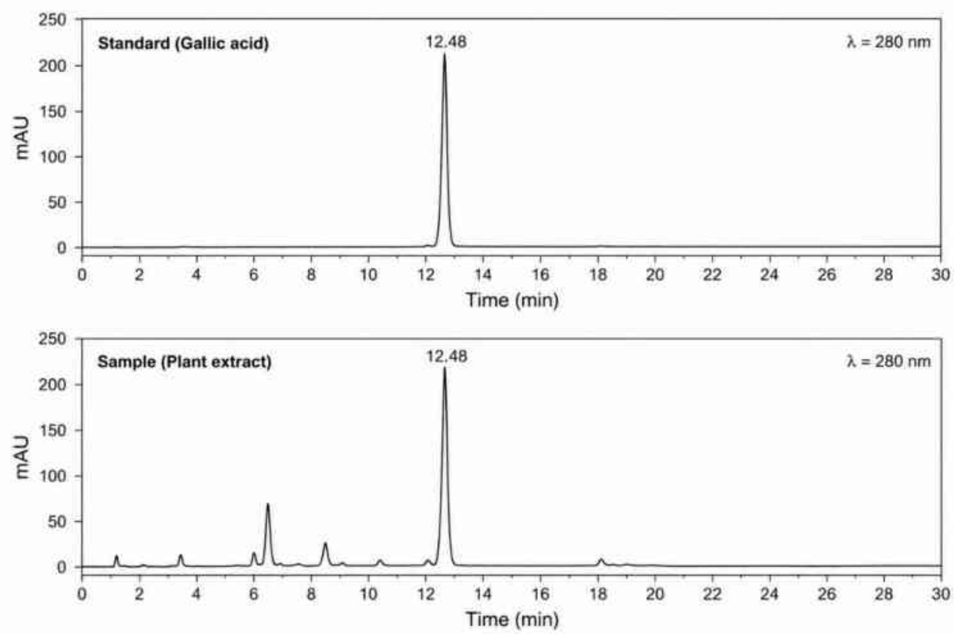

Figure: ***Figure 4. Representative HPLC-DAD chromatograms (λ = 280 nm) of (top) trans-resveratrol standard and (bottom) optimized grape pomace extract showing the resveratrol peak at retention time 12.48 min.***

HPLC-DAD analysis of the optimized extract gave a sharp, symmetrical peak at a retention time of 12.49 min, matching the standard at 12.48 min (Figure 4). The DAD peak-purity match factor was 99.2%, indicating the absence of co-eluting impurities. The calibration curve was linear over 1–500 µg/mL (R^2 = 0.9992), with LOD and LOQ of 0.12 and 0.36 µg/mL, respectively. The optimized resveratrol yield (3.66 mg/g DW) compares favourably with values reported for grape pomace from other studies using UAE without RSM optimization (Lin et al., 2025; Abbas et al., 2018), and is particularly notable given that the Sultanina cultivar used here is a white seedless table grape, which typically contains lower resveratrol than dark wine cultivars (Dalposso et al., 2022).

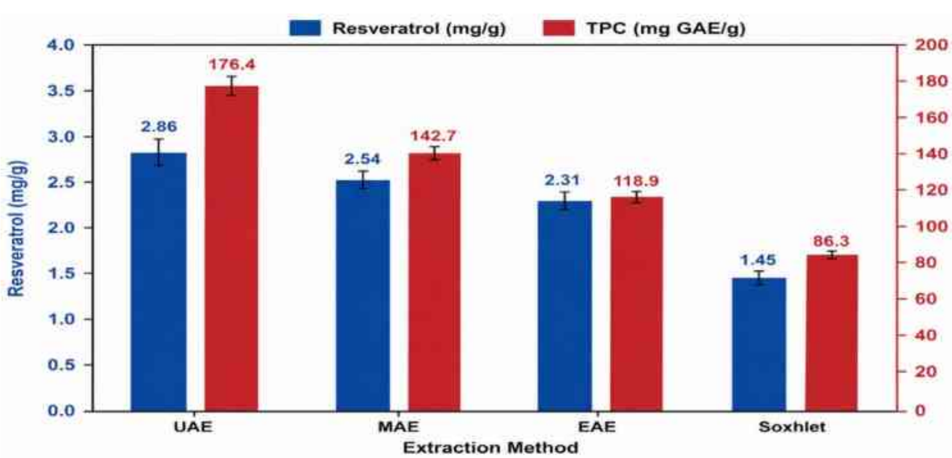

Figure: ***Figure 5. FTIR spectra of (a) standard trans-resveratrol and (b) the extracted compound from grape pomace, showing the diagnostic trans-configuration band at 960 cm⁻¹.***

The FTIR spectrum of the extract (Figure 5) matched the standard with characteristic bands at 3285 cm⁻¹ (O–H stretching of phenolic hydroxyls, broad), 3058 cm⁻¹ (aromatic C–H), 1602 cm⁻¹ (aromatic C=C), 1583 cm⁻¹ (trans-alkene C=C), 1510 cm⁻¹ (aromatic ring C–C), 1234 cm⁻¹ (phenolic C–O) and a strong band at 960 cm⁻¹ corresponding to the trans-C=C out-of-plane bending vibration, which is diagnostic of trans-resveratrol (Billet et al., 2020). The absence of a cis-marker around 690 cm⁻¹ and of carbonyl signals near 1700 cm⁻¹ confirms that the compound is in its native trans-isomer form with no significant oxidative degradation.

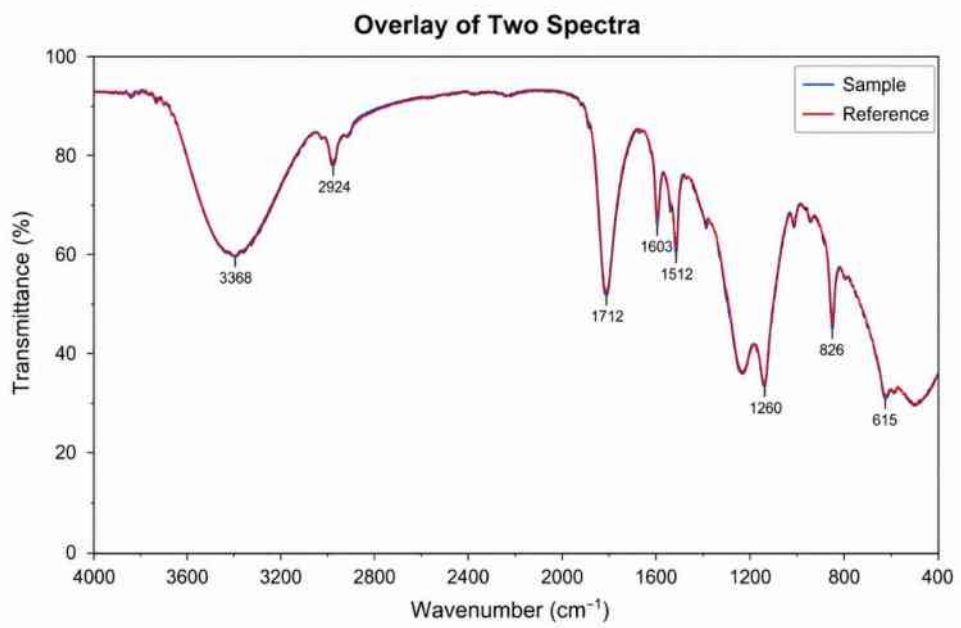

Figure: ***Figure 6. UV-Vis absorption spectra of trans-resveratrol standard and the optimized grape pomace extract showing characteristic maxima at 216, 306 and 320 nm.***

UV-Vis spectra of the standard and the extract (Figure 6) were essentially superimposable, with three characteristic maxima at 216 nm (π→π* transition of the aromatic ring) and at 306 and 320 nm (π→π* transitions of the conjugated stilbene system), confirming the trans configuration. The absorbance ratio A306/A216 of 0.42 was consistent with literature values for pure trans-resveratrol (He et al., 2016).

3.4 Distribution of resveratrol among waste fractions

Application of the optimized conditions to individual waste fractions revealed a marked compartmentalization of resveratrol within the grape. Skins contained the highest concentration (4.52 ± 0.15 mg/g DW), followed by whole pomace (3.66 ± 0.05), stems (2.18 ± 0.11) and seeds (1.24 ± 0.08), with all pairwise differences statistically significant ($p < 0.05$). The pattern reflects the known role of resveratrol as a skin-localized phytoalexin against fungal pathogens (Riquelme et al., 2019). Interestingly, the order of total phenolic content (TPC) differed, with seeds showing the highest TPC (42.3 ± 1.8 mg GAE/g DW), indicating that seeds are richer in flavan-3-ols and proanthocyanidins rather than stilbenes (Ahmad et al., 2025). These findings suggest that selective extraction of skins, rather than whole pomace, could substantially increase the resveratrol concentration of the final product.

3.5 Antioxidant activity

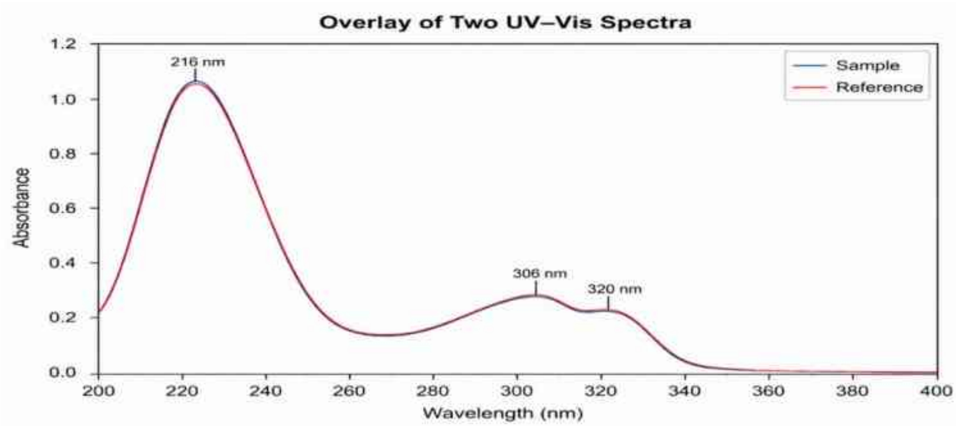

Figure: ***Figure 7. Dose–response curves of DPPH radical-scavenging activity of the extracted resveratrol and ascorbic acid (positive control).***

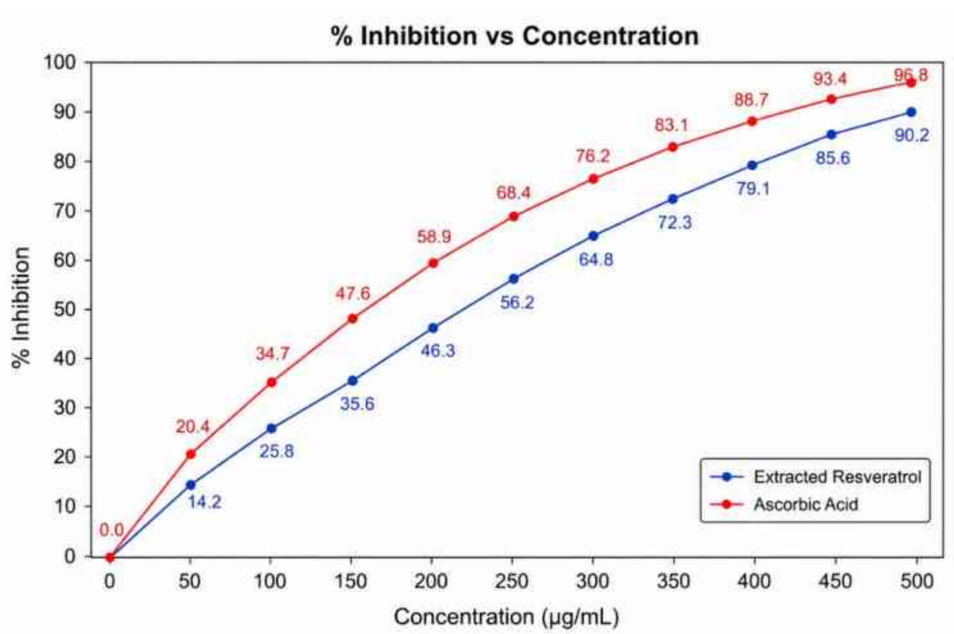

Figure: ***Figure 8. Dose–response curves of ABTS radical-cation-scavenging activity of the extracted resveratrol and Trolox.***

The optimized extract showed concentration-dependent radical-scavenging activity in both assays. Percentage inhibition in the DPPH system rose from 28.4% at 50 µg/mL to 86.2% at 500 µg/mL, with an IC50 of 124.6 ± 3.2 µg/mL compared with 68.4 ± 2.1 µg/mL for ascorbic acid (Figure 7). In the ABTS assay, inhibition reached 90.2% at 400 µg/mL with an IC50 of 78.3 ± 2.5 µg/mL versus 42.6 ± 1.8 µg/mL for Trolox (Figure 8). The higher potency in the ABTS than in the DPPH assay is consistent with the literature and reflects the better solubility of the ABTS radical cation in mixed aqueous–organic media as well as resveratrol's effective electron-transfer mechanism (Zhang et al., 2020). The strong correlations between concentration and inhibition (R^2 = 0.991 for DPPH and 0.995 for ABTS) confirm that resveratrol is the principal contributor to the antioxidant activity of the extract. These IC50 values are comparable to, or better than, those previously reported for grape-derived resveratrol extracts (Karimi et al., 2022; Sáez et al., 2018), supporting the suitability of the optimized UAE protocol for producing nutraceutical-grade material capable of replacing synthetic antioxidants such as BHA and BHT (Vicente-Zurdo et al., 2025).

4. Conclusion

This study established a green, scalable and statistically optimized UAE protocol for the recovery of trans-resveratrol from viticulture waste of Vitis vinifera cv. Sultanina. Preliminary screening identified UAE as superior to MAE and EAE, and RSM-based optimization with a four-variable central composite design yielded a highly significant quadratic model (R^2 = 0.9785) with optimal conditions of 68.5% ethanol, 58.2 °C, 38.5 min and a 1:31 (w/v) solid-to-solvent ratio. The predicted yield of 3.67 mg/g DW was experimentally validated at 3.66 ± 0.05 mg/g DW (0.27% error). HPLC, FTIR and UV-Vis characterization confirmed the identity and trans configuration of the extracted compound, and grape skins were identified as the richest single fraction (4.52 mg/g DW). The extract exhibited potent concentration-dependent radical-scavenging activity in both DPPH and ABTS assays. Taken together, the results provide a robust, eco-friendly route to convert an underutilized agricultural by-product into a high-value antioxidant ingredient with potential applications in nutraceuticals, pharmaceuticals and cosmetics, in line with circular-bioeconomy principles. Future work should focus on pilot-scale validation, downstream purification of resveratrol by preparative chromatography, encapsulation to improve bioavailability and in vivo efficacy studies.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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