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Assessment of Bioactive Phenolic Compounds in Musts and the Corresponding Wines of White and Red Grape Varieties

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Abstract: Wine contains important amounts of antioxidants, which contribute to the protection of the body from oxidative stress and associated diseases. This study aims to characterize the bioactive characteristics and individual polyphenolic composition of different white and red musts and the corresponding wines obtained at Stefanesti vineyard, Romania, and to observe the evolution of the main phenolic compounds from the musts to the corresponding wines. General bioactive characteristics (total polyphenols, total tannins, total catechins, total anthocyanins contents, total tannin, and antioxidant activity) were determined using UV-Vis spectrometric methods, while phenolic composition (phenolic acids, flavonoids, and stilbenes) was detected using UHPLC–HRMS analysis. The fermentation and stabilization processes that occur during the transformation of musts into the corresponding wines lead to a decrease in the general bioactive characteristics from musts to wines, while the fermentation of the musts leads to an enrichment of the individual phenolic compounds in the corresponding wines, with a significant increase in the content of gallic, syringic, and p-coumaric acids in the wines compared with the musts. A clear distinction of the musts and wines was obtained for both white and red varieties, indicating different phenolic compositions of the musts and wines. The obtained results contribute to the characterization of the polyphenolic fingerprint of the investigated white and red musts and wines.

Keywords: wine; must; anthocyanins; catechin; polyphenolic compounds; tannins; antioxidant activity; UHPLC–ESI/HRMS

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1. Introduction

Plant-derived phytochemicals found in fruits, vegetables, seeds, spices, and derived food products, including functional foods that we consume daily [1–3], but also in fruits and vegetable by-products [4], are responsible for aroma, color, and antioxidant properties. Among phytochemicals, polyphenols are becoming increasingly important due to their beneficial effects on health associated with their role as natural antioxidants [5–7].

Grapevine is one of the major fruit crops that is cultivated on large areas all over the world [8,9], with the resulting grapes and wines containing important amounts of phytochemicals and nutrients that provide numerous health benefits [10,11]. Polyphenols represent the most important phytochemicals in grapes and the corresponding wines as they are associated with numerous biological activities and health benefits [12,13] due to polyphenols antioxidant properties and their ability to eliminate free radicals [14,15]. Of these, we mention the reduction in the incidence of diseases such as cardiovascular and

neurological diseases, atherosclerosis and high blood pressure, metabolic syndrome, cancer, and type 2 diabetes [16,17].

The polyphenolic composition of the grapes depends on the species (*Vitis vinifera, Vitis labrusca*, and *Vitis rotundifolia*) and grape varieties [18,19]. Among polyphenols, phenolic acids, flavonoids, anthocyanins, stilbenes, lignans, and polymerized forms, such as tannins and lignins, are representative for grapes and the derived products, including musts and wines [20,21]. The majority of all grapes (*Vitis vinifera*) are used in winemaking, and some varieties are consumed as table grapes [22,23]. The amounts of phenols extracted from grapes into wines depend on the chemical composition of the grape skin [24,25]. The polyphenolic profiles of the grapes and the wines depend on several factors, such as grape variety and maturity, environmental factors (soil, climate), agricultural practice, winemaking technology, and the conditions of aging the wine [26,27]. The distribution of polyphenols varies in different parts of the grape berry, such as anthocyanins and tannins which are found in the skin and pro-anthocyanidins which are found in skins and seeds, while phenolic acids are predominant in the pulp [12]. In the making of red wine, the must is fermented together with the skins of the grapes, the pulp, and the seeds, while in white wine, it occurs only by the fermentation of grape juice without the skins of the grapes [19,24]. Consequently, tannins and anthocyanins are the major polyphenols in red wines, whereas phenolic acids are the most abundant in white wines [19,28]. The presence of various phenolic compounds in wine's composition determines its ultimate character [20]. Consequently, anthocyanins are responsible for color [29,30], flavonols and hydroxycinnamic acid derivatives are responsible for stabilizing young red wines by co-pigmentation, and flavan-3-ols are responsible for wine astringency and bitterness [31,32].

Considering all these premises, the aim of this study was to investigate the individual phenolic composition in terms of hydroxybenzoic, hydroxycinnamic, and chlorogenic acids, flavanols, flavonols, and the associated bioactive characteristics of different white and red musts and the corresponding wines obtained under the winemaking and terroir characteristics of the Stefanesti vineyard, Romania. The evolution of the main phenolic compounds from musts to wines and varieties with a high antioxidant potential associated with the polyphenolic composition is also highlighted in this study.

2. Materials and Methods

2.1. Grape Musts and Their Wine Samples

The investigated musts and wines were obtained from *Vitis vinifera* grapes, including white varieties (Fetească Regală, Riesling Italian, Sauvignon Blanc, and Muscat Ottonel) and red varieties (Merlot, Burgund Mare, and Cabernet Sauvignon), grown at the Ştefăneşti vineyard, Argeș County (44°51′ N and 24°57′ E). The pedoclimatic characteristics of the vineyard are specific for umbrisol soils, with loamy-sandy and loamy-clay textures, without skeleton. The studied area is characterized by a favorable climate for grape cultivation, with moderate temperatures, long sunshine, and rainfall occurring in the summer (Table S1). The grapes were harvested manually at full maturity in the 2021 harvest year. The grapes were subjected to winemaking technology specific to white and red wines. The white grapes were debarked, crushed, and pressed, after which the must (grape juice) was placed in fermentation containers. The red grapes were subjected to the winemaking technology for red wine (debarked, crushed, and the must, pulp, and grape skins placed in rotating containers to ferment on the log for 10 days). Representative samples were taken from the musts and stored in tubes at −20 °C until analysis. Duplicate samples of each, white and red young wines, were collected after 10 days from the malolactic fermentation and were then subjected to determinations.

2.2. Chemicals and Reagents

Folin–Ciocalteu phenol reagent (pure) was purchased from Carl ROTH GmbH Co. (Karlsruhe, Germany), radical scavenging assay reagents DPPH (95% 1,1-diphenyl-2-picryhidrazyl) were purchased from Acros Organics (Slovakia), Trolox 97% (6-hydroxy-

2,5,7,8-tetramethyl-2-carboxylic acid) was obtained from Alfa Aesar (Thermo Fisher GmbH Kandel, 76870 Kandel, Germany), gallic acid and vanillin were purchased from Carl ROTH GmbH Co. (Karlsruhe, Germany), and H_2SO_4 96% and HCl 37% were from Chemical Company (Bucharest, Romania). All chemicals and solvents used in chromatography were obtained from Carl Roth GmbH Co. (Karlsruhe, Germany) and Merck Co. (Darmstadt, Germany), and they were of HPLC or analytical grade (>99%) quality. The analytical standards of phenolic acids (gallic, p-coumaric, caffeic, chlorogenic, ferulic, 4-hydroxibenzoic, 3,4-dihidroxibenzoic, t-cinnamic, and syringic), flavanols ((+)-catechin, and (−)-epicatechin), flavonols (quercetin, kaempferol, isorhamnetin, chrysin, pinocembrin, apigenin, and galangin), t-resveratrol, and ellagic and abscisic acids were purchased from Sigma-Aldrich (Steinheim, Germany).

2.3. Analytical Determinations

2.3.1. UV-Vis Spectrophotometric Determinations

Spectrophotometric determinations (total polyphenols—TPFs, total catechins—TCs, total tannins—TTs, total anthocyanins—TAs, and antioxidant activity—AA) of the musts and wines were conducted using an Analytik Jena Specord 205 UV/VIS spectrophotometer (Analytik Jena GmbH, Jena, Germany) equipped with 1 cm path length glass and quartz cells.

Total polyphenols (TPFs) were determined via the colorimetric Folin–Ciocalteu method, using gallic acid as a reference standard [33,34], measuring the maximum absorbance at 760 nm. In a 100 mL volumetric flask, the following were inserted in order, wine sample (1 mL of white wine and 1 mL red wine diluted 1/5, respectively), 50 mL of distilled water, 5 mL of Folin–Ciocalteu reagent, and 20 mL of sodium carbonate 20% (*m*/*v*) solution, and these were brought to the mark with distilled water. We then stirred in order to achieve homogenization. After 30 min, the absorbance was measured at 760 nm against a blank prepared with distilled water instead of wine. TPF quantification was based on the standard curve obtained with a serial dilution of a gallic acid standard solution in the range of 50–1000 mg/L of gallic acid (r^2 value of the standard curve: 0.9900). The values were expressed as mg gallic acid equivalents (GAE)/L of must or wine.

Catechins (TCs) are monomer flavanolic units (proanthocyanidins), and total catechins are determined via a proanthocyanin-specific test using 1% alcoholic vanillin solution; when a reaction occurs, that leads to the appearance of the red color, which then becomes stable in concentrated solutions of HCl [35]. Briefly, 10 mL of wine or must were combined with 10 mL of 11.5 N HCl and 5 mL of 1% vanillin solution, and after 20 min, the absorbances were measured at 500 nm against ultrapure water. A calibration curve using standard catechin solutions covering the range of 0.02–0.1 mg/L was used to express the quantitative values in mg/L (r^2 value of the standard curve: 0.9846).

Tannins (TTs) were determined based on their property to change into cyanidin in a strongly acidic environment combined with a high temperature [35]. In two tubes, 2 mL of wine/must was combined with 4 mL of a 27.75% HCl solution, and then one of the tubes was boiled for 45 min while the other was kept at 20 °C. After cooling the tube, the color was stabilized with 0.5 mL of concentrated H_2SO_4, and then the optical density of the boiled and unboiled solutions was measured at 520 nm. The results were calculated using the following formula:

$$\text{TT (mg/L)} = ((15.7 \times \Delta\text{OD520}) \times \text{V} \quad (1)$$

where the reading of ΔDO520 nm (the difference between the boiled and the unboiled sample) was at wavelength 520, and V denotes the volume of must or wine.

Anthocyanins (TAs) determination is based on their property to react with SO_2, forming colorless products. We prepared the mixture using the following instructions: add 1 mL of filtered wine or must, 1 mL of HCl 0.1%, and 20 mL of HCl 2%. From this mixture, two solutions were prepared which were put into two tubes with the following composition: solution 1 (5 mL of mixture and 2 mL of distilled water) and solution 2 (5 mL of mixture

and 2 mL of solution of sodium metabisulphite 16%). After 20 min, the optical densities of solutions 1 and 2 were measured against distilled water at a wavelength of 520 nm in 1 cm path length glass cells [36]. The quantitative results were calculated using the following formula:

$$\text{TA (mg/L)} = \Delta\text{DO520} \times 875 \quad (2)$$

where ΔDO520 is the difference in the two solutions at wavelength DO520.

DPPH Assay (AA). The antioxidant activity was determined using the method reported by Geana et al. [37] with some modifications. An aliquot of 0.1 mL of must/wine was mixed with 3.9 mL of DPPH• methanolic solution (2.5×10^{-2} mg/L methanolic DPPH solution). The resulting solutions were homogenized and were then incubated for 45 min whilst protecting them from light. The absorbance was measured at 517 nm using methanol as a reference. The results were calculated based on an external standard method using Trolox solutions covering the range of 50–1500 mg/L (r^2 value of the standard curve: 0.9869), and the results were expressed as mmol Trolox equivalents (TE)/L of must/wine.

2.3.2. Individual Phenolic Composition by UHPLC-ESI/HRMS

The quantitative profiles of individual phenolic acids, flavonoids, and stilbenes in the investigated musts and wines were obtained by conducting a UHPLC-HRMS analysis (ultra-high-performance liquid chromatography combined with high-resolution mass spectrometry) using a high-resolution Q Exactive mass spectrometer™ Focus Hybrid Quadrupole—OrbiTrap equipped with HESI, coupled to an UltiMate 3000 UHPLC system (Thermo Fisher Scientific, San Jose, CA, USA). A Kinetex C18 column (100 × 2.1 mm, 1.7 µm particle diameter) was used for the chromatographic separation of phenolic compounds at 30 °C under a gradient elution of two mobile phases, A (0.1% formic acid in water) and B (0.1% formic acid in methanol), at a 0.3 and 0.4 mL/min flow rate, as presented before [38]. The data were obtained in full negative scan mode in the range of m/z 75–1000 with a power of resolution of 70,000 FWHM at m/z 200. Different isolation windows (75–205 m/z, 195–305 m/z, 295–405 m/z, 395–505 m/z, and 495–1000 m/z) were used in variable data-independent analysis MS^2 (vDIA) at a resolution of 35,000. The ionization parameters were as follows: 11 and 48 arbitrary units for collision and auxiliary nitrogen, 2.5 kV applied voltage, a capillary temperature of 320 °C, and 30 EV collision energy. Xcalibur software package (Version 4.1) (Thermo Fisher Scientific, San José, CA, USA) was used for data processing. The identification of phenolic compounds was performed by comparing the retention times and mass spectra with those of the authentic standards, and the results were calculated based on the external standard method and expressed in mg/L.

2.4. Data Processing

The analyses were conducted in duplicate. Statistical differences between the bioactive composition of the musts and the corresponding wines were tested using the Duncan test (multiple t test) at a 0.05 significance level ($p \leq 0.05$), while Pearson's correlation test was performed to highlight correlations between the variables. Principal component analysis (PCA) was performed to discriminate between different white (Feteasca Regală, Riesling Italian, Sauvignon Blanc, and Muscat Ottonel) and red (Burgund Mare, Merlot, and Cabernet Sauvignon) musts and wines and to identify specific phenolic biomarkers. Microsoft Excel 2010 (Microsoft, Redmond, WA, USA) and XLSTAT Add in soft version 15.5.03.3707 (Addinsoft, New York, NY, USA) were used to perform the mathematical and statistical analyses.

3. Results and Discussion

3.1. Bioactive Characteristics of the White and Red Grape Musst and Wines

The content of bioactive compounds in grape musts was compared with that of the corresponding wines. Therefore, to determine differences between the bioactive compounds, must–wine interaction was analyzed for the four white and red varieties, highlighted by variance analysis, using the Duncan test ($p \leq 0.05$). Figure 1 shows a significant difference

between the polyphenolic compounds in white musts and wines, demonstrating that fermentation results in the loss of polyphenols. It is noted that, among the varieties taken into study, the must and wine of the Feteasca Regală variety have the highest total polyphenols contents (563.67 mg GAE/L of must and 471.4 mgGAE/L of wine). Consequently, the antioxidant activity was also the highest, at 12.4294 mmol TE/L. The lowest total polyphenols content corresponds to Riesling Italian must (413.97 mgGAE/L) and Sauvignon Blanc wine (343.29 mmol TE/L), while lower values of antioxidant activity correspond to both must and wine of Sauvignon Blanc. The concentration of tannins in white musts is low, ranging between 10.44 mg/L in the Italian Riesling variety and 15.65 mg/L in the Feteasca Regala variety, while in white wines they were not found due to the white wines' winemaking technology, which only briefly allows contact of the grape juice with the skin. Red musts and wines contain high amounts of tannins, with values between 1414.97 and 4726.6 mg/L in musts and between 1362.7 and 4121.0 mg/L in wines, with higher values corresponding to Merlot must and wine.

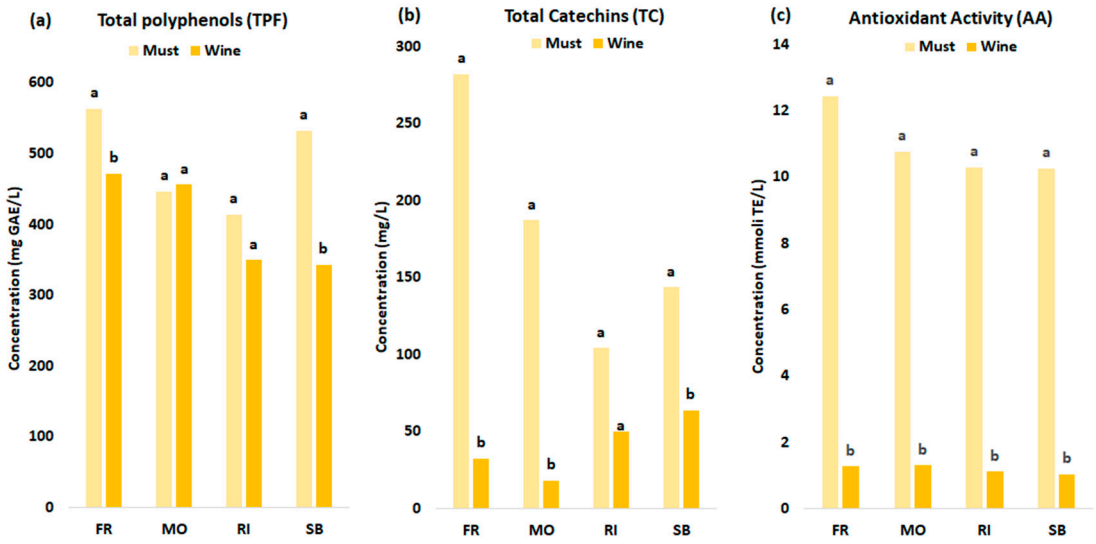

Figure 1. Bioactive characteristics of must and wines of white grape varieties (FR—Feteasca Regală; RI—Riesling Italian; MO—Muscat Ottonel; SB—Sauvignon Blanc): (**a**) Total polyphenols (TPFs) (mg GAE/L); (**b**) total catechins (TCs) (mg catechins/L); and (**c**) antioxidant activity (AA) (mmol TE/L). Different lowercase letters in each graph indicate a significant difference at $p < 0.05$ according to Duncan's multiple range test.

Compared to the literature data, the total polyphenols contents of the investigated wines were similar to Chardonnay wine (445 mg GAE/L [39] or 379 mg GAE/L [40]) and Italian Riesling (303 mg GAE/L) [41], but they were higher than Sauvignon (262 mg GAE/L) and Terret Sauvignon (289 mg GAE/L) [40], as well as Feteasca Regală (230 mg GAE/L) [16] (Table S2). The antioxidant activity in the literature is close to that obtained in the must and wine from white grapes, specifically Riesling Italian must/wine (8.40/0.09 mmol TE/L) [19] and Fetească Regală wine (0.93 mmol TE/L) [16] (Table S2).

The catechin content in white musts ranged between 104.30 and 282.10 mg catechins/L, with lower values corresponding to the Riesling Italian variety and higher values corresponding to the Feteasca Regala variety. For wines, the catechin content ranged between 18.17 and 63.79 mg catechin/L, with a lower amount in the Muscat Ottonel variety and a higher amount in the Sauvignon Blanc variety (Figure 1). The TCs of the studied white wines were comparable with the literature data for Chardonnay wine (28.7 mg/L), Sauvignon (27.9 mg/L), and Viognier (38.35 mg/L) [40] (Table S2).

According to the Duncan test, significant differences ($p \leq 0.05$) between the bioactive properties (TPFs, TCs, TTs, AA) of white musts and the corresponding wines were observed for Feteasca Regala and Sauvignon Blanc varieties, mostly based on TPFs and TCs (Figure 1),

while no significant differences were observed in the case of Muscat Ottonel and Riesling Italian musts and wines.

The total polyphenols content in red grape musts varied from 3338.89 mg GAE/L for the Cabernet Sauvignon variety to 5611.11 mg GAE/L for the Burgund Mare variety, while the measured values in the corresponding wines varied from 2192.39 mg GAE/L for the Cabernet Sauvignon variety to 2937.10 mg GAE/L for the Merlot variety (Figure 2). The total polyphenolic content of the studied red wine varieties was comparable with the available literature data (e.g., 1750.9–2424.1 mg GAE/L) [42] (Table S2). The antioxidant activity of the red musts and wines ranged from 18.95 to 24.31 mM TE/L for musts and from 14.29 to 15.62 mm TE/L for wines, with higher values corresponding to Burgund Mare must and Merlot wine, respectively (Figure 2). The obtained values of AA were slightly higher than those reported by Burin et al. (7.49–11.36 mm TE/L) [42], but slightly lower than the literature data for Cabernet Sauvignon (14.4–21.39 mM TE/L) and Merlot (10.75–19.50 mM/L) wines [39] (Table S2). Total anthocyanins (TAs) of the red musts were higher than those of the corresponding wines, with significantly higher values of TAs in Merlot must and wine (Figure 2). The TAs content of the Cabernet Sauvignon and Burgund Mare wines were comparable with the literature data (358.3–887.6 mg/L) [42] (Table S2).

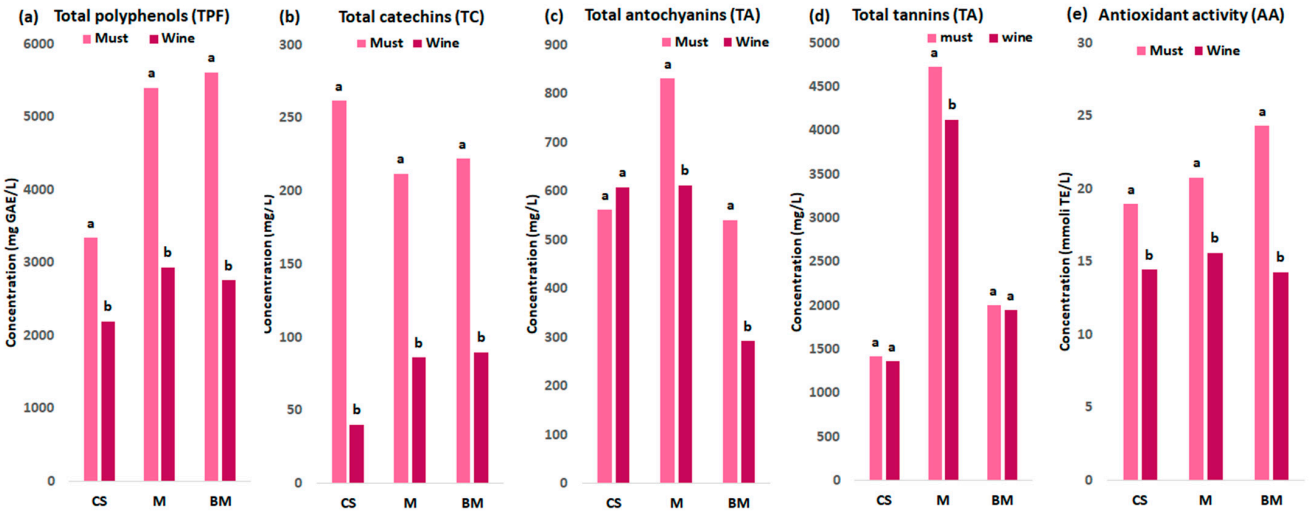

Figure 2. Bioactive characteristics of must and wines of red grape varieties (BM—Burgund Mare; CS—Cabernet Sauvignon; M—Merlot): (**a**) Total polyphenols (TPFs) (mg GAE/L); (**b**) total catechins (TCs) (mg catechins/L); (**c**) total anthocyanins (TAs) (mg/L); (**d**) total tannins (TTs) (mg/L); and (**e**) antioxidant activity (AA) (mmol TE/L). Different lowercase letters in each graph indicate a significant difference at $p < 0.05$ according to Duncan's multiple range test.

The total tannins (TTs) of the studied red must varieties were comparable, while significantly lower TCs were observed for Cabernet Sauvignon (1362.70 mg/L) and Burgund Mare (1944.00 mg/L) wines compared with Merlot wine (4121.00 mg/L). The studied literature data reported TTs ranging from 1037 to 1726 mg/L for Shiraz wine, 1066 to 2261 mg/L for Cabernet Sauvignon, and 789 to 1750 mg/L for Merlot wines [39]. The total catechins (TCs) of the red musts varied between 211.69 and 261.79 mg/L, while for the resulting wines, they varied between 40.12 and 89.57 mg/L, values lower than those reported for Cabernet Sauvignon (172.1 mg/L), Merlot (128.8 mg/L), and Syrah (149.1 mg/L) wines [40]. According to the Duncan test, significant differences ($p \leq 0.05$) between red musts and the corresponding wines were observed only based on TPFs (Figure 2), while no significant differences were observed based on the other parameters.

In the case of white varieties, Pearson's correlation analysis (Table 1) shows positive correlations between the bioactive properties of the investigated grape musts and their corresponding wines. All the correlation coefficients were higher than 0.5. A strong positive correlation was observed for antioxidant activity, with the total tannin content and total

catechin, demonstrating the importance of these two categories of parameters in perfecting the taste and flavor of white wines. Additionally, a strong correlation was observed between the TCs and TTs of the white musts and wines.

Table 1. Pearson's correlation analysis between the bioactive properties of white varieties of must and wine.

Variables	TPFs	TCs	TTs	AA
TPFs (mg GAE/L)	**1**	0.628	0.658	0.626
TCs (mg/L)	0.628	**1**	**0.902**	**0.878**
TTs (mg/L)	0.658	**0.902**	**1**	**0.992**
AA (mM TE/L)	0.626	**0.878**	**0.992**	**1**

Total polyphenols (TPFs) (mg GAE/L), total catechins (TCs) (mg catechins/L), total tannins (TTs) (mg/L), and antioxidant activity (AA) (mmol TE/L) in the musts and wines of white grape varieties (FR—Feteasca Regală; RI—Riesling Italian; MO—Muscat Ottonel; SB—Sauvignon Blanc). Pearson's correlation values in bold are significant at $p < 0.05$.

The total polyphenols content in red musts and wines is significantly positively correlated with antioxidant activity, followed by positive but weak correlations with the content of catechins, anthocyanins, and tannins (Table 2). In turn, the antioxidant activity is strongly correlated with the total catechin content and poorly correlated positively with the total anthocyanin and tannin contents.

Table 2. Pearson's correlation analysis between the bioactive properties of red varieties of must and wine.

Variables	TPFs (mg GAE/L)	Tas (mg/L)	TCs (mg/L)	TTs (mg/L)	AA (mM TE/L)
TPFs (mg GAE/L)	**1**	0.450	0.722	0.401	**0.936**
Tas, mg/L	0.450	**1**	0.292	0.622	0.382
TCs, mg/L	0.722	0.292	**1**	0.052	**0.822**
TTs, mg/	0.401	0.622	0.052	**1**	0.144
AA, mM TE/L	**0.936**	0.382	**0.822**	0.144	**1**

Total polyphenols (TPFs) (mg GAE/L), total catechins (TCs) (mg catechins/L), total tannins (TTs) (mg/L), and antioxidant activity (AA) (mmol TE/L) in the musts and wines of red grape varieties (BM—Burgund Mare; CS—Cabernet Sauvignon; M—Merlot). Pearson's correlation values in bold are significant at $p < 0.05$.

3.2. Individual Phenolic Compounds in White and Red Grape Must and Wine by UHPLC–ESI/HRMS

Identification and quantification of the polyphenolic compounds were performed by UHPLC–ESI/HRMS analysis using an external calibration method. A typical total ion current (TIC) chromatogram is shown in Figure S1 for the Burgund Mare grape must. The retention time, the name of the compound, the formula, the m/z values of the adduct ions, and the MS/MS fragment ions in negative ESI mode, the mass error, and the exact molecular mass are given in Table 3.

The quantitative results of individual phenolic compounds in musts and wines of different white and red varieties are presented in Table 4. It is obvious that the individual phenolic compounds were quantified in higher amounts in red musts and wines compared with white musts and wines and, in general, the amounts of phenolic compounds increase in wines compared with the corresponding musts.

Table 3. The identification of phenolic compounds in grape must and wine by UHPLC–ESI/HRMS with structures confirmed by comparison with reference standards.

No	Compound	Retention Time (min)	Formula	Exact Mass	Accurate Mass $(M-H)^-$	Experimental Adduct Ion (*m*/*z*)	Mass Fragments
	Phenolic acids						
1	Gallic acid	1.94	$C_7H_6O_5$	170.0215	169.0142	169.0133	125.0231
2	3,4-Dihydroxybenzoic acid	4.25	$C_7H_6O_4$	154.0266	153.0193	153.0184	109.0281
3	4-Hydroxybenzoic acid	6.96	$C_7H_6O_3$	138.0316	137.0243	137.0233	118.9650, 96.9588, 71.0124
4	t-Ferulic acid	8.89	$C_{10}H_{10}O_4$	194.0579	193.0506	193.0499	178.0262, 134.0361
5	Chlorogenic acid	7.90	$C_{16}H_{18}O_9$	354.0950	353.0877	353.0880	191.0553
6	Caffeic acid	7.98	$C_9H_8O_4$	180.0422	179.0349	179.0343	135.044
7	Syringic acid	8.39	$C_9H_{10}O_5$	198.0528	197.0455	197.0450	182.0212, 166.9976, 153.0547, 138.0311, 123.0075
8	Cinnamic acid	8.37	$C_9H_8O_2$	148.0524	147.0451	147.0439	119.0489, 103.0387
9	Ellagic acid	9.71	$C_{14}H_6O_8$	302.0062	300.9989	300.9993	300.9990
10	p-Coumaric acid	8.69	$C_9H_8O_3$	164.0473	163.0400	163.0389	119.0489
Flavonoids							
11	Catechin	7.53	$C_{15}H_{14}O_6$	290.0790	289.0717	289.0716	109.0282, 123.0349, 125.0232, 137.0232, 151.0390, 203.0708
12	Epi-catechin	8.12	$C_{15}H_{14}O_6$	290.0790	289.0717		
13	Quercetin	10.68	$C_{15}H_{10}O_7$	302.2357	301.0354	301.0351	151.0226, 178.9977, 121.0282, 107.0125
14	Isorhamnetin	11.79	$C_{16}H_{12}O_7$	316.0582	315.0509	315.0510	300.0277
15	Kaempferol	11.60	$C_{15}H_{10}O_6$	286.0477	285.0404	285.0403	151.0389, 117.0180
16	Apigenin	11.83	$C_{15}H_{10}O_5$	270.0528	269.0455	269.0455	117.0333, 151.0027, 107.0126
17	Pinocembrin	12.54	$C_{15}H_{12}O_4$	256.0735	255.0662	255.0660	213.0551, 151.0026, 107.0125
18	Chrysin	13.43	$C_{15}H_{10}O_4$	254.0579	253.0506	253.0506	143.0491, 145.0284, 107.0125, 209.0603, 63.0226, 65.0019
19	Galangin	13.58	$C_{15}H_{10}O_5$	270.0528	269.0455	269.0454	169.0650, 143.0491
20	Pinocembrin	14.77	$C_{16}H_{14}O_4$	270.0892	269.0819	269.0822	179.0554
Stilbens							
21	t-Resveratrol	9.97	$C_{14}H_{12}O_3$	228.0786	227.0713	227.0708	185.0813, 143.0337

Among the determined compounds (Table 4), it is noted that syringic, gallic, and 3,4-dihydroxybenzoic acids, catechin, and epicatechin were quantified in higher amounts, mostly in red musts and wines. Phenolic acids, among the syringic, gallic, and 3,4-dihydroxybenzoic acids, have various properties, including antioxidant, antifungal, antimicrobial, anti-inflammatory, and anticancer properties [19,43]. The amount of syringic acid quantified in white varieties varied from n.d. to 0.02 mg/L in musts and from 7.03 to 42.51 mg/L in wines, while in the case of red varieties, the amount of syringic acid ranged between 0.04 and 2732 mg/L in musts and between 188.7 and 590.7 mg/L in wines, the obtained values being much higher compared with the literature data [16].

Gallic acid was quantified in lower amounts in musts than in corresponding wines, for both white and red varieties, with values ranging between n.d.–0.64 mg/L and 0.82–4.24 mg/L in white musts and wines and between 0.01–28.84 mg/L and 17.70–89.12 mg/L for red musts and wines, with higher values corresponding to Muscat Ottonel and Burgund Mare wine varieties. The obtained values were lower compared with the literature data for white [44] and red [44–46] wines, except for both the must and wine of the Burgund Mare variety. The amounts of 3,4-dihydroxybenzoic were higher in red musts and wines (n.d. –0.72 mg/L for musts and 3.94–24.25 mg/L for wines) compared with white musts and wines (0.07–0.26 mg/L for musts and 0.05–0.93 mg/L for wines). Significantly higher amounts of syringic acid were quantified in red musts and wines (0.04–273.2 mg/L for musts and 188.7–590.7 mg/L for wines) and white wines (7.03–42.51 mg/L) compared with the literature data (n.d.–2.05 mg/L for white wines and 1.01–43.57 mg/L for red wines) (Tables S3 and S4). Additionally, the amounts of ferulic and p-coumaric acids increase from musts to wines for both white and red varieties, with higher amounts of ferulic and p-coumaric acids corresponding to BM and CS red wines, values that are higher [44,46] or

comparable [47] with the available literature data. The amounts of t-cinnamic acid decrease from musts to wines, especially in the case of white varieties, with values ranging from 0.32 to 3.16 mg/L in white musts and from 0.01 to 0.30 mg/L in corresponding wines. Caffeic acid was quantified only in the musts, while in the wines it was not detected.

Table 4. Concentration of phenolic compounds (mg/L) in musts (m) and wines (w) of different white (FR—Fetească Regală, MO—Muscat Ottonel, RI—Risling Italian, SB—Sauvignon Blanc) and red (M—Merlot, CS—Cabernet Sauvignon, B—Burgund Mare) varieties.

Phenolic Compounds (mg/L)	White Varieties								Red Varieties					
	FR m	FR w	MO m	MO w	RI m	RI w	SB m	SB w	BM m	BM w	CS m	CS w	M m	M w
Gallic acid	0.19 ^{e}	2.24 ^{b}	n.d. ^{e}	4.24 ^{a}	0.11 ^{e}	1.66 ^{c}	0.64 ^{d}	0.82 ^{d}	28.84 ^{C}	89.1 ^{A}	0.03 ^{E}	17.70 ^{D}	0.01 ^{F}	30.89 ^{B}
3,4-dihydroxybenzoic acid	0.07 ^{f}	0.93 ^{a}	0.08 ^{e,f}	0.59 ^{b}	0.13 ^{e}	0.05 ^{f}	0.26 ^{c}	0.19 ^{d}	0.72 ^{D}	15.44 ^{B}	n.d. ^{D}	3.94 ^{C}	n.d. ^{A}	24.52 ^{A}
4-hydroxibenzoic acid	0.02 ^{d}	0.07 ^{b}	0.05 ^{c}	0.11 ^{a}	0.03 ^{c,d}	0.07 ^{b,c}	0.09 ^{b}	0.06 ^{c}	0.35 ^{C}	0.78 ^{B}	n.d. ^{C,D}	2.35 ^{A}	n.d. ^{D}	0.60 ^{B}
Chlorogenic acid	0.03 ^{a}	0.05 ^{a}	n.d. ^{a}	n.d. ^{a}	0.03 ^{a}	0.04 ^{a}	0.01 ^{a}	0.01 ^{a}	0.07 ^{D}	0.16 ^{B,C}	n.d. ^{D}	0.44 ^{A}	n.d. ^{C}	0.20 ^{B}
Syringic acid	0.01 ^{e}	15.63 ^{c}	0.01 ^{e}	42.51 ^{a}	0.02 ^{e}	17.66 ^{b}	n.d. ^{e}	7.03 ^{d}	273.22 ^{C}	590.76 ^{A}	0.27 ^{E}	188.76 ^{D}	0.04 ^{E}	444.40 ^{B}
p-coumaric acid	0.01 ^{d,e}	1.12 ^{a}	n.d. ^{e}	0.13 ^{c,d}	0.03 ^{d,e}	1.33 ^{a}	0.18 ^{c}	0.53 ^{b}	0.78 ^{C,D}	18.27 ^{A}	n.d. ^{D}	17.04 ^{B}	n.d. ^{D}	2.27 ^{C}
Ferulic acid	0.02 ^{c}	0.35 ^{a}	n.d. ^{c}	0.02 ^{c}	0.03 ^{c}	0.22 ^{b}	0.03 ^{c}	0.26 ^{a}	0.70 ^{C}	9.81 ^{A}	n.d. ^{C}	5.46 ^{B}	n.d. ^{C}	0.24 ^{C}
Caffeic acid	0.03 ^{b}	n.d. ^{b}	n.d. ^{b}	n.d. ^{b}	0.07 ^{b}	n.d. ^{b}	0.52 ^{a}	n.d. ^{b}	1.89 ^{A}	n.d. ^{D}	1.07 ^{B}	n.d. ^{D}	0.44 ^{C}	n.d. ^{D}
Cinnamic acid	0.32 ^{d}	0.06 ^{e}	3.16 ^{a}	0.01 ^{e}	2.01 ^{b}	0.24 ^{d}	1.93 ^{c}	0.30 ^{d}	1.63 ^{A}	1.29 ^{B}	n.d. ^{C}	1.56 ^{A}	n.d. ^{C}	1.65 ^{A}
Catechin	3.64 ^{a}	0.04 ^{g}	n.d. ^{g}	3.01 ^{c}	2.69 ^{d}	3.43 ^{b}	2.35 ^{e}	1.75 ^{f}	51.54 ^{A}	23.66 ^{C}	0.05 ^{E}	0.19 ^{D}	0.03 ^{E}	1.03 ^{E}
Epi-catechin	1.03 ^{c}	0.01 ^{d}	n.d. ^{d}	1.23 ^{c}	1.12 ^{c}	2.98 ^{a}	2.28 ^{b}	0.89 ^{c}	44.94 ^{A}	5.11 ^{D}	0.04 ^{B}	0.17 ^{E}	0.02 ^{C}	0.43 ^{E}
Quercetin	2.00 ^{b}	n.d. ^{e}	1.49 ^{c}	0.51 ^{d}	1.52 ^{c}	n.d. ^{e}	9.44 ^{a}	n.d. ^{e}	239.70 ^{A}	12.30 ^{B}	0.24 ^{C}	0.16 ^{E}	0.01 ^{D}	0.67 ^{E}
Kaempferol	0.01 ^{a}	n.d. ^{a}	n.d. ^{a}	0.01 ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	0.05 ^{A}	0.71 ^{A}	n.d. ^{A}	0.12 ^{A}	n.d. ^{A}	0.09 ^{A}
Isorhamnetin	0.02 ^{a}	n.d. ^{a}	n.d. ^{a}	0.03 ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	0.74 ^{A}	0.48 ^{A}	n.d. ^{A}	0.03 ^{A}	n.d. ^{A}	0.05 ^{A}
Apigenin	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	0.01 ^{A}	0.02 ^{A}	n.d. ^{A}	0.06 ^{A}	n.d. ^{A}	0.06 ^{A}
Pinocembrin	n.d. ^{a}	0.01 ^{a}	n.d. ^{a}	0.01 ^{a}	n.d. ^{a}	0.01 ^{a}	n.d. ^{a}	0.01 ^{a}	n.d. ^{A}	0.07 ^{A}	n.d. ^{A}	0.61 ^{A}	n.d. ^{A}	0.54 ^{A}
Chrysin	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	0.01 ^{A}	0.05 ^{A}	n.d. ^{A}	0.03 ^{A}	n.d. ^{A}	0.04 ^{A}
Galangin	0.01 ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	n.d. ^{a}	0.01 ^{A}	0.02 ^{A}	n.d. ^{A}	0.07 ^{A}	n.d. ^{A}	0.10 ^{A}
Resveratrol	0.44 ^{b,c}	0.02 ^{d}	n.d. ^{d}	0.35 ^{c}	0.70 ^{a}	0.06 ^{d}	0.54 ^{a,b}	0.01 ^{d}	5.77 ^{A}	3.13 ^{B}	0.01 ^{C}	1.28 ^{E}	n.d. ^{D}	3.00 ^{B,C}
Ellagic acid	0.06 ^{a}	0.12 ^{a}	0.02 ^{a}	0.09 ^{a}	0.04 ^{a}	0.01 ^{a}	0.03 ^{a}	0.01 ^{a}	0.65 ^{A}	0.49 ^{A}	n.d. ^{A}	0.69 ^{A}	n.d. ^{A}	0.45 ^{A}
Abscisic acid	0.05 ^{d,e}	0.14 ^{a,b,c,d}	0.09 ^{c,d}	0.02 ^{e}	0.09 ^{b,c,d}	0.13 ^{a,b,c}	0.15 ^{a,b}	0.14 ^{a}	0.25 ^{A}	0.86 ^{A}	n.d. ^{B}	0.73 ^{A}	n.d. ^{C}	0.17 ^{C}
∑phenolic compounds	8.03	20.74	4.9	52.93	8.56	27.89	17.93	12.01	650.02	772.56	0.64	241.42	0.11	511.4

The letters represent the different groups from the interactions between the different varieties of white (lowercase letters in the row) and red (uppercase letters in the row) musts and wines according to Duncan's multiple range test at $p \leq 0.05$; n.d.—not detected.

Generally, the (+)-catechin and (−)-epicatechin contents decrease from musts to wines, indicating that those compounds are reduced by fermentation processes, especially in the case of FR, SB, and B varieties. Higher amounts of (+)-catechin and (−)-epicatechin correspond to B must (m) and wine (w) (51.54 (m)/23.66 (w) mg/L for (+)-catechin and 44.94 (m)/5.11 (w) mg/L for (−)-epicatechin), values lower than those found in Feteasca Neagra wine [16] and similar to those found in Cabernet Sauvignon, Merlot, and Pinot Noire red wines [45,46,48].

Quercetin, kaempferol, apigenin, chrysin, and galangin are flavonols that are found more in leaves and fruits than in wine; these compounds are quantified in musts but, in most cases, are not detected in wines. Among those flavonoids, quercetin was quantified in higher amounts in B must (239.7 mg/L) and wine (12.30 mg/L), followed by SB must (9.44 mg/L) (Table 3). The literature data indicate higher amounts of quercetin in Cabernet Sauvignon (4.57–5.46 mg/L) and Merlot (4.65–5.78 mg/L) wines [44,48] compared with the data of this study.

t-Resveratrol, a biosynthesized polyphenol of various plants and fruits with a powerful antioxidant potential [49], was quantified in both musts and wines, with values between n.d.–0.70 mg/L and 0.01–0.35 mg/L in white musts and wines, while higher amounts were quantified in red musts (n.d.–5.77 mg/L) and wines (1.28–3.13 mg/L). The amounts of t-resveratrol quantified in the investigated white and red wines were lower compared with the literature data for white [46,50] and red [19,50] wines.

Among the white musts, higher total quantified phenolic compounds (∑phenolic compounds) correspond to SB must, followed by RI, FR, and MO musts, while in the obtained wines, higher total quantified phenolic compounds correspond to MO wines, followed by RI and FR white wines. BM red must and wine show higher total quantified phenolic compounds, followed by M and CS wines.

3.3. Discrimination of the White and Red Musts and the Corresponding Wines

Unsupervised multivariate statistical analysis (PCA) was performed in order to discriminate between different white and red musts and the corresponding wines and to identify specific phenolic biomarkers for each category. In the case of white varieties, PCA based on the main bioactive characteristics (TPFs, TCs, TTs, TAs, and AA) explained 96.23% of the total variation using two main components, with a higher contribution brought by PC1 (84.10%) compared to PC2 (12.13%) (Figure 3a). From the plot map (Figure 3a), white wines are grouped separately from their musts on either side of the PC1 axis, and positive correlations have been achieved between all the bioactive characteristics of white musts, with TPFs characterizing SB must and TCs, TTs, and AA characterizing RI and MO musts.

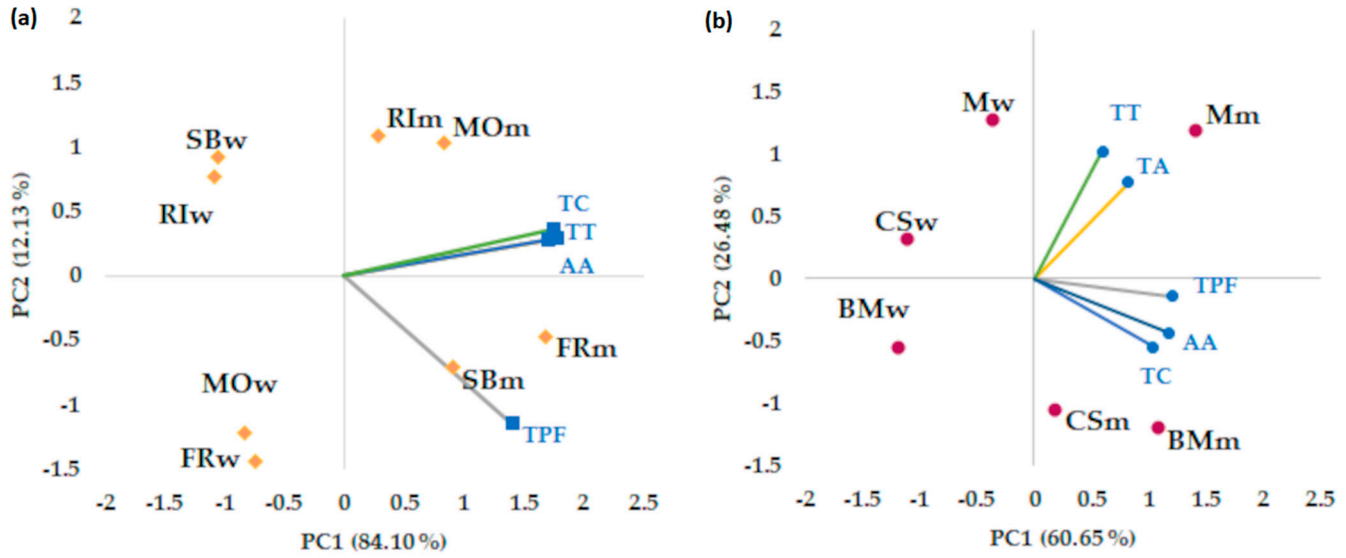

Figure 3. Discrimination of musts (m) and the corresponding wines (w) based on the main bioactive characteristics (TPFs, TCs, TTs, TAs and AA): (**a**) white varieties (SBm/v—Sauvignon Blanc must/wine, RIm/w—Riesling Italian must/wine, MOm/w—Muscat Ottonel must/wine, FRm/w—Feteasca Regala must/wine) and (**b**) red varieties (Mm/w—Merlot must/wine, CSm/w—Cabernet Sauvignon must/wine, BMm/w—Burgund Mare must/wine).

In the case of red varieties, the PCA explained 87.13% of the overall variation using two main components, with PC1 (60.65%) contributing more than PC2 (26.48%) (Figure 3b). Similar to the white varieties, the red musts and wines were clearly distinguished, with M must defined by TTs and TAs characteristics, while CS and BM musts are characterized by TPFs, TCs, and AA (Figure 3b).

Considering individual phenolic compounds, similar discrimination pathways were observed for white and red varieties; PCA analysis explained 59.36% of the total variation in the case of white varieties (Figure 4) and 74.2% of the total variation in the case of red varieties (Figure 4). From the score plot map, it is noted that white musts were grouped on the right side of the PC1 axis, and the corresponding wines were grouped on the left side (Figure 4a). Along the PC1 axis, the white musts are correlated with caffeic (CafA), chlorogenic (ChlA), and t-cinnamic (CinA) acids, flavonoids (isorhamnetin—iRh, kaempferol—Kae, chrysin—Chry, galangin—Ga, quercetin—Qu), (+)-catechin (Cat) and (−)-epicatechin (ECat), and t-resveratrol—Res, while white wines are correlated with pheno-

lic acids (syringic—SyA, gallic—GaA, 3,4-dihidroxibenzoic—3,4-DHBA, 4-hydroxibenzoic—4-HBA, p-coumaric—p-CoumA, ferulic—FA) and abscisic (AbsA) and ellagic (ElA) acids (Figure 4b).

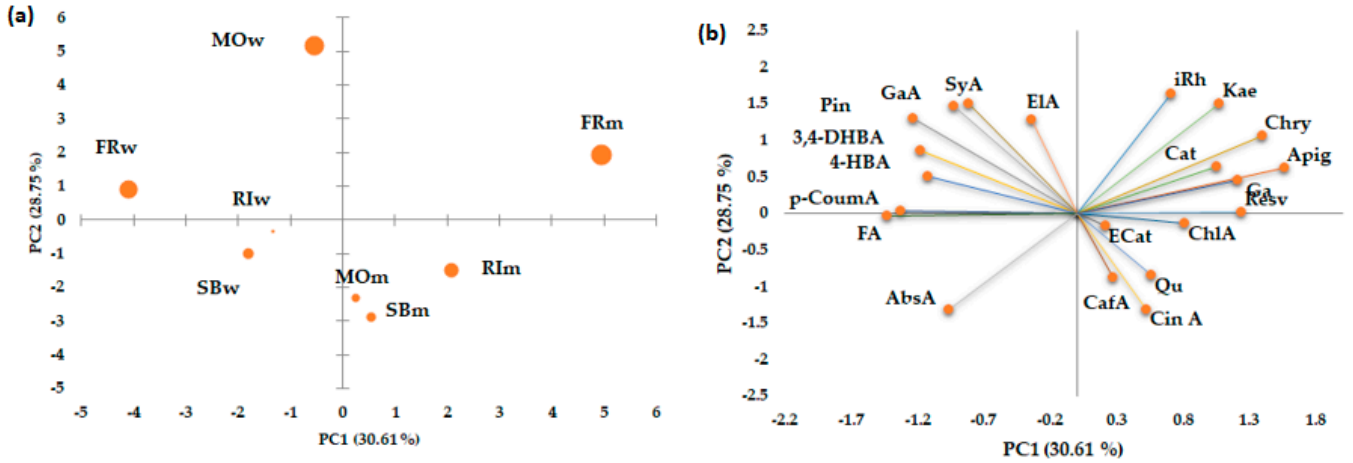

Figure 4. Discrimination of white musts and wines based on individual phenolic compounds: (**a**) Score plot of the first two discriminant functions showing separation between different white musts and wines (SBm/v—Sauvignon Blanc must/wine, Rim/w—Riesling Italian must/wine, Mom/w—Muscat Ottonel must/wine, FRm/w—Feteasca Regala must/wine) and (**b**) correlation between the individual phenolic compounds (3,4-dihydroxybenzoic acid (3,4-DHBA), 4-hydroxybenzoic acid (4-HBA), gallic acid (GA), syringic acid (SyA), caffeic acid (CafA), p-coumaric acid (p-Coum), ferulic acid (FA), cinnamic acid (CinA), chlorogenic acid (ChlA), abscisic acid (AbsA), ellagic acid (ElA), (+)-catechin (Cat), (−)-epicatechin (Ecat), quercetin (Qu), kaempferol (Kae), isorhamnetin (iRh), apigenin (Apig), pinocembrin (Pin), chrysin (Chry), galangin (Ga), t-resveratrol (Res)) and the factors.

In the case of red varieties, the PCA explained 74.20% of the overall variation using the main components, with PC1 (48.35%) contributing more than PC2 (25.85%) (Figure 5a). The red musts were grouped on the right side of the PC1 axis, whereas the corresponding wines were grouped on the left, indicating a clear difference in the phenolic composition of musts versus wines. It is observed that the Burgund Mare variety (B) can be distinguished from other red varieties in both musts and wines (CS and M). PCA analysis also revealed that red musts are well correlated with flavonoids (Qu, Kae, iRh, Apig, Chry, Ga), Cat, and ECat, CafA, and Res, while red wines are well correlated with phenolic acids (SyA, GaA, CinA, p-CoumA, 3,4-DHBA, 4-HBA, FA, ChlA) (Figure 5b).

Pearson's correlation analysis applied on quantitative data reveals strong and moderate correlations between the main phenolic compounds in musts and wines. The correlation coefficient with values greater than 0.5 was used to interpret the correlation coefficient with values greater than 0.5.

In the case of white varieties, strong positive correlations were observed between gallic acid and syringic and 4-hydroxibenzoic acids and pinocembrin, between caffeic acid and quercetin, syringic acid and pinocembrin, between (+)-catechin and (−)-epicatechin, between p-coumaric acid and ferulic acid, and also between kaempferol and isorhamnetin, apigenin and chrysin, and between galangin and apigenin (Table S5). Strong negative correlations were observed between abscisic acid and kaempferol, isorhamnetin and chrysin, and between quercetin and pinocembrin (Table S5), indicating the same origin sources for the correlated phenolic compounds. In addition to white varieties, strong positive correlations were observed for (+)-catechin and (−)-epicatechin with caffeic acid, t-resveratrol, quercetin, kaempferol, and isorhamnetin (Table S6).

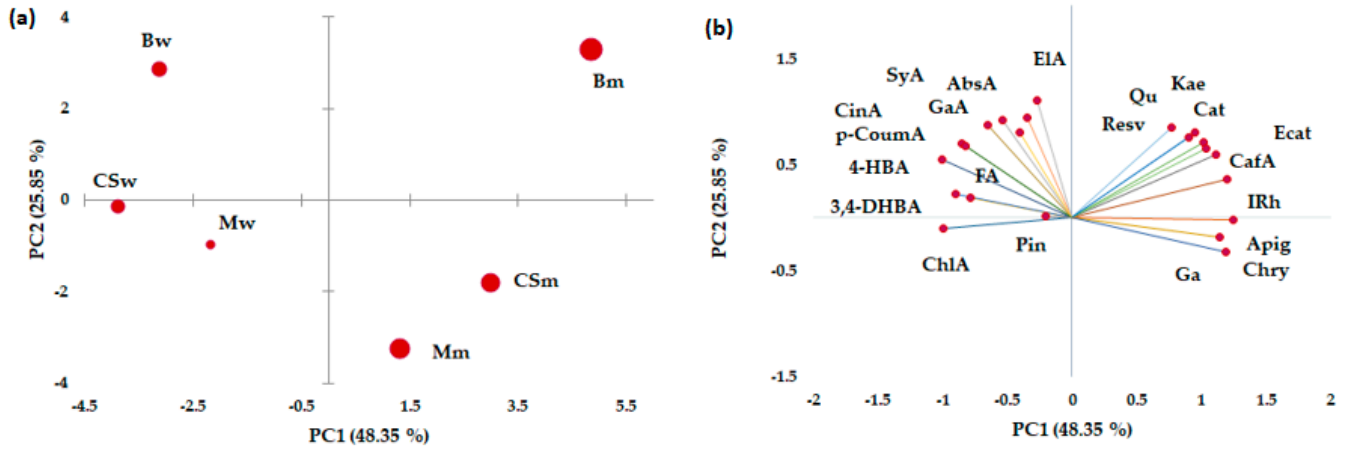

Figure 5. Discrimination of red musts and wines based on individual phenolic compounds. (**a**) Score plot of the first two discriminant functions showing separation between different red musts and wines (Mm/w—Merlot must/wine, CSm/w—Cabernet Sauvignon must/wine, BMm/w—Burgund Mare must/wine) and (**b**) correlation between the individual phenolic compounds (3,4-dihydroxybenzoic acid (3,4-DHBA), 4-hydroxybenzoic acid (4-HBA), gallic acid (GA), syringic acid (SyA), caffeic acid (CafA), p-coumaric acid (p-Coum), ferulic acid (FA), cinnamic acid (CinA), chlorogenic acid (ChlA), abscisic acid (AbsA), ellagic acid (ElA), (+)-catechin (Cat), (−)-epicatechin (ECat), quercetin (Qu), kaempferol (Kae), isorhamnetin (iRh), apigenin (Apig), pinocembrin (Pin), chrysin (Chry), galangin (Ga), t-resveratrol (Res)) and the factors.

This study provides significant data addressing the evolution of phenolic compounds from musts to wines of different white and red varieties. In general, the fermentation processes of white and red musts lead to an enrichment of phenolic compounds in the wines compared with the musts. Thus, the increase in the content of gallic, syringic, and p-coumaric acids in wines compared with musts were much more obvious in the case of red varieties. Contrary, the amounts of some phenolic compounds (caffeic and t-cinnamic acids, (+)-catechin, (−)-epicatechin, quercetin, and t-resveratrol) decreased after the fermentation process, being quantified in lower amounts in wines compared with musts.

4. Conclusions

This study presents a detailed characterization of the main bioactive characteristics and phenolic compounds content of different musts and their corresponding wines obtained from white and red grape varieties. PCA analysis based on the quantitative data (bioactive characteristics and individual phenolic composition) allows a discrimination to occur between musts and wines, as well as between white and red varieties. Some phenolic compounds (caffeic and t-cinnamic acids, (+)-catechin, (−)-epicatechin, quercetin, and t-resveratrol) are lost through alcoholic fermentation and thus show lower values in wines compared musts, whereas the amounts of other phenolic compounds (gallic, syringic, and p-coumaric acids) increase in wines compared with musts. Pearson's correlation analysis shows strong and moderate correlations between the main phenolic compounds in musts and wines. In summary, the information presented here could serve as a valuable database for further research aimed at investigating the polyphenolic composition of different musts and wines to optimize farming practices in the vineyard and the winemaking process so as to obtain wines with a high content of bioactive compounds.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app13095722/s1, Figure S1: The obtained total ion current (TIC) chromatogram for the separation of polyphenolic compounds in Burgund Mare grape must by UHPLC–ESI/HRMS; Table S1: The viticultural climate of the vegetation and maturation period corresponding to Stefanesti vineyard during the 2021 harvest year; Table S2: Content of total phenolic compounds (TPC, expressed as mg GAE/l), total anthocyanins (TA, expressed in mg/L),TC—total

catechins—catechine/ flavonoid content mg/L, TT-tannins (expressed in mg/L), AA-antioxidant activity (expressed in mMol Trolox/l) in wine and grape must; Table S3: Phenolic compounds in white grape musts (m) and wines (w) (mg/L); Table S4: Phenolic compounds in red grape musts (m) and wines (w) (mg/l); Table S5: Correlation matrix and Pearson coefficients of determination for individual phenolic compounds in must and wine for white grape cultivars; Table S6: Correlation matrix and Pearson coefficients of determination for individual phenolic compounds in must and wine for red grape cultivars. References [16,19,39–42,44–48,50–52] are cited in the Supplementary Materials.

Author Contributions: Conceptualization, P.A.O. and E.-I.G.; methodology, P.A.O. and E.-I.G.; software, A.F. and E.-I.G.; validation, E.-I.G., P.A.O. and C.T.C.; formal analysis, P.A.O., C.T.C. and E.-I.G.; investigation, P.A.O., A.F., E.-I.G. and C.T.C.; resources, D.I.S. and R.E.I.; data curation, P.A.O. and E.-I.G.; writing, P.A.O., E.-I.G., A.F. and C.T.C.; writing—review and editing, P.A.O., E.-I.G. and A.F.; visualization, R.E.I., D.I.S. and O.T.; supervision, R.E.I., D.I.S. and O.T.; project administration, R.E.I. and D.I.S. All authors have read and agreed to the published version of the manuscript.

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