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The Effects of Drying and Grinding on the Extraction Efficiency of Polyphenols from Grape Skin: Process Optimization

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Abstract: Maximizing the yield of bioactive molecules extracted from plant materials requires the investigation of extraction process variables; therefore, in this research, a traditional aqueous solid–liquid extraction method was employed on two distinct grape pomace skin samples. The grape skin pomace represents a potentially valuable source of biologically active compounds, particularly polyphenols. Experiment 1 utilized ground grape pomace skin, whereas experiment 2 utilized grape pomace skin that had been both dried and ground beforehand. Employing a Box–Benkhen experimental design and response surface modeling in the Statistica 14.0 software package, this study evaluated the impact of temperature, extraction time, solid-to-liquid ratio (S/L), and mixing speed on extraction efficiency. The extracted compounds were assessed for both physical properties (conductivity, total dissolved solids, and pH) and chemical properties (total polyphenol content and antioxidant activity using 2,2-Diphenyl-1-picrylhydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) assays). The optimization matrix design identified the specific conditions required to achieve the optimal physical and chemical properties of grape skin extract as follows: (i) for experiment 1, extraction time (t) = 15 min, temperature (T) = 80 °C, solid-to-liquid ratio (S/L) = 10 g/L, and mixing speed (rpm) = 500 1/min and (ii) for experiment 2, extraction time (t) = 15 min, temperature (T) = 80 °C, solid-to-liquid ratio (S/L) = 10 g/L, and mixing speed (rpm) = 375 1/min. Under optimal process conditions, 26.1284 $mg_{GAE}/g_{d.m.}$ and 25.1024 $mg_{GAE}/g_{d.m.}$, respectively, were obtained. These findings demonstrate the effectiveness of the optimization process in identifying precise extraction conditions that yield the optimal chemical properties of grape skin extracts.

Keywords: drying; grape skin; extraction condition optimization; grinding; polyphenol aqueous extraction; response surface modeling

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1. Introduction

Grape pomace, the main solid organic waste generated during wine production, is estimated to produce approximately 1 kg of pomace for every 6 L of wine produced. Globally, annual pomace production is estimated at around 9 million tons [1], with Croatia alone producing about 40,600 tons [2]. The composition of grape pomace mainly consists of grape skin, seeds, and stems, with their proportions influenced by factors such as grape variety, maturity, climate, and processing methods [3]. Red grape pomace is separated after partial fermentation, while white grape pomace is separated before fermentation begins. The chemical composition of pomace is influenced by various factors, including the vinification or fermentation method, grape variety, harvest year, climatic conditions, geographical origin, cultivation method, storage method, and isolation technique, making comparisons between studies challenging [4].

Pomace moisture content typically ranges from 50% to 72% and varies based on grape variety and ripeness [4]. Lignin constitutes 16.8% to 24.2% of pomace components, while protein accounts for less than 4% [5]. Pectin compounds account for 37% to 54% of the total

polysaccharides in grape cell walls, while cellulose makes up the remaining 27% to 37% of polymeric components. Various products such as ethanol, tartrate, citric acid, oil, hydrocolloid, and dietary fiber can be extracted from grape pomace. Additionally, grape pomace is rich in polyphenols (like resveratrol, anthocyanins, flavones, and tannins) that remain in the grape pomace during grape processing, and it can serve as an unconventional source of pectin [4]. Specified properties make the grape pomace an interesting raw material for the food industry. Several papers on the valorization of grape pomace have been published in the last few years. For example, Megías-Pérez et al. [6] optimized pectin extraction from grape pomace, and Filippi et al. [7] used grape pomace as the substrate for succinic acid production using the bacterial strain *Actinobacillus succinogenes*, while Elejade et al. [8] analyzed the potential of polyphenol supplementation for exercise-induced oxidation stress. Also, the effect of the addition of grape pomace to food products like bread [9–11], cookies [12], muffins [9,13], and/or biscuits [14,15] has been extensively analyzed. Grape pomace has also been used for the fortification of meat and fish products [16,17], as well as the fortification of dairy products [18,19].

Phenolic compounds are abundant and diverse natural products found in plants, exhibiting a wide range of physiological properties, including anti-allergic, anti-inflammatory, antimicrobial, antioxidant, cardioprotective, and vasodilating effects [20]. Many phenolic compounds have been identified in grape pomace, with anthocyanins, hydroxybenzoic and hydroxycinnamic acids, flavan-3-ols, flavonols, and stilbenes being the most prevalent [21,22].

Classical solid–liquid extraction serves as the basis for many analytical procedures in sample preparation [23]. Maximizing the yield of bioactive molecules extracted from plant materials requires the investigation of extraction process variables. Solvent extraction is favored for extracting bioactive molecules as it allows the recovery of thermally sensitive materials at low temperatures [24]. Extraction efficiency is influenced by variables such as temperature, solvent type, extraction time, solid-to-liquid ratio, and the sample's chemical composition and physical characteristics [25]. The solvent choice is critical, with commonly used solvents including water, methanol, ethanol, acetone, ethyl acetate, and aqueous alcohol solutions. The solvent choice affects both the amount and rate of polyphenol extraction [26]. Organic solvents used in plant extraction are typically those with boiling temperatures below 80 °C and exhibit low reactivity, low viscosity, cost-effectiveness, suitability for reuse, and heat, oxygen, and light stability, safety, and availability [27]. Considering these criteria, water emerges as a suitable solvent for solid–liquid extraction processes, being a low-cost, non-dangerous polar solvent capable of effectively extracting a broad range of phenolic molecules with notable antioxidant properties originating from a variety of plant sources [28].

Statistical and mathematical modeling techniques have been successfully utilized to analyze variables significant for extracting bioactive molecules from plant materials and predict optimal extraction conditions [29]. Traditional one-variable-at-a-time methods are time-consuming, expensive, and fail to consider the interaction effects of components, thus being less reliable. The Response Surface Methodology (RSM) addresses these limitations by simultaneously evaluating multiple factors and how they interact with one or more response variables, lowering the number of experimental procedures needed to extract bioactive substances [30–33]. There are several examples of the optimization of polyphenol extraction from grape pomace. For example, Moutinho et al. [34] applied the RSM to optimize polyphenol extraction from two grape varieties, taking into consideration the ethanol concentration, extraction temperature, and extraction pH. Ćurko et al. [35] optimized the effect of methanol concentration, temperature, and extraction time on the microwave-assisted extraction of different groups of polyphenolic compounds from grape skin pomace, while Putnik et al. [36] optimized the different acidities and extraction time effects on flavonoid recovery from grape skin pomace (*Vitis vinifera* L. cv. Merlot).

Based on the previously mentioned research gap, the primary goal of this study was to identify the ideal conditions for the conventional aqueous solid–liquid extraction of bioac-

tive compounds from dried and ground grape skin using the Box–Behnken experimental design and RSM modeling. The novelty of this study lies in its systematic application of the Box–Behnken design and RSM modeling to optimize the extraction process, potentially transforming grape skin, a typically discarded byproduct, into a valuable source of bioactive compounds. This approach not only contributes to waste reduction but also adds economic value to the food industry by utilizing a resource that is often considered unprofitable.

2. Materials and Methods

2.1. Materials

2.1.1. Grape Skin Samples

This study analyzed the pomace skin of white Graševina grapes (*Vitis vinifera* cv. Graševina) harvested in Kutjevo, Croatia in 2021. To ensure consistency, the pomace was stored at −18 °C before experimentation. The seeds were separated from the skin before analysis. In order to establish a consistent sample, all batches were blended together to reduce the effects of variability within the pomace. The dry matter content of the grape skin was determined based on the AOAC method [37]. The physical and chemical characteristics of the grape skin used in the extraction experiments were as follows: moisture content of 65.07%, pH of 4.60, and C/N ratio of 32.16.

2.1.2. Chemicals and Reagents

The following materials were acquired from Sigma-Aldrich Chemie (St. Louis, MO, USA): 2,4,6-tris(2-pyridyl)-striazine (TPTZ), gallic acid (≥98% purity), iron (II) sulphate heptahydrate, 1,1-diphenyl-2-picrylhydrazyl (DPPH), and 6-hydroxy-2,5,7,8-tetramethylchromane-2 carboxylic acid (Trolox). Gram-Mol d.o.o. (Zagreb, Croatia) supplied the sodium carbonate, 30% hydrochloric acid, and hexahydrate iron (III) chloride. J.T. Baker (Deventer, The Netherlands) provided the sodium acetate trihydrate. The Folin–Ciocalteu reagent was sourced from Kemika d.d., located in Zagreb, Croatia. Acetic acid was supplied by T.T.T. d.o.o. in Sveta Nedjelja, Croatia. Methanol was obtained from Carlo Erba Reagents S.A.S. (Peypin, France).

2.2. Methods

2.2.1. Grape Skin Pretreatments

Grape skin, both fresh and dried at T = 50 °C for 24 h, was ground using an IKA Tube Mill (IKA Werk GmbH & Co. KG, Staufen, Germany) at a blade rotation speed of rpm = 15,000 1/min. The grinding time was adjusted according to the size of the particles to be obtained (t = 10–40 s). Both fresh grape skin and grape skin that had been previously dried were ground to a particle size ranging from 100 to 300 µm. The experimental procedure is presented in Figure 1.

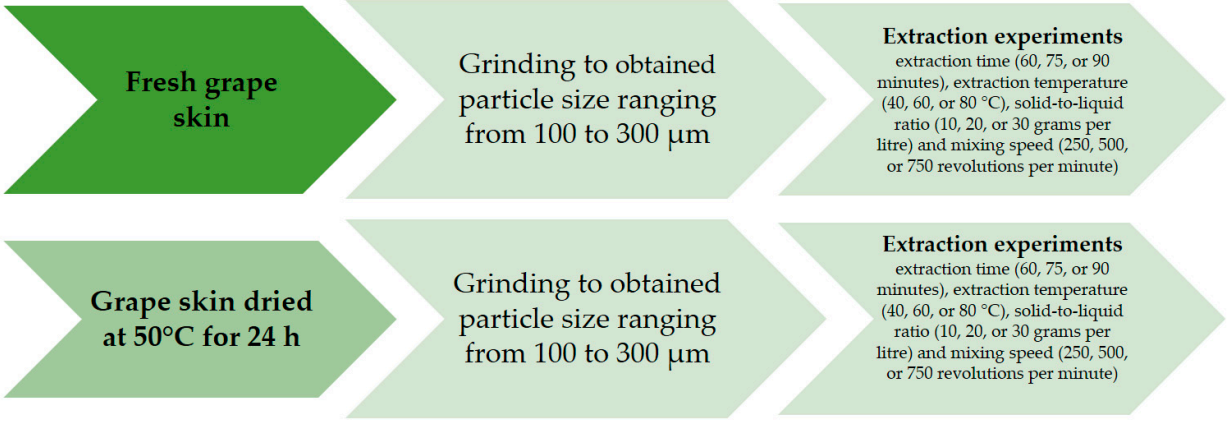

Figure 1. Experimental procedure.

2.2.2. Extraction Experiments

The experiments were performed according to the Box–Behnken design previously described by Sokač Cvetnić et al. [38]. This experimental design examined the impact of four variables on the extracts' polyphenol production: extraction time (60, 75, or 90 min), extraction temperature (40, 60, or 80 °C), solid-to-liquid ratio (10, 20, or 30 g per liter) and mixing speed (250, 500, or 750 revolutions per minute). The experimental conditions were selected based on the available data in the literature [39]. The extraction experiments were performed in a laboratory oil bath (IKA-Werk GmbH & Co. KG, Staufen, Germany) with precise control of the temperature and mixing speed. Following the specified extraction period, the mixture was filtered through a cellulose paper filter (pore size of 5–13 µm, LLG Labware, Meckenheim, Germany) in order to isolate the solid material from the liquid extract that contained polyphenols. Then, the physical and chemical characteristics of the extracts were examined.

2.2.3. Physical Properties of the Grape Skin Extracts

The pH values of the aqueous extracts were determined using a pH meter (Model 914, Metrohm, Switzerland). A conductometer (SevenCompact, Mettler Toledo, Switzerland) was used to test the extracts' conductivity and total dissolved solids. The AOAC method was used to evaluate the extraction yield [37]. The physical properties were measured three times, with mean values ± standard deviations reported for each measurement.

2.2.4. Total Phenolic Content and Antioxidant Activity of the Grape Skin Extracts

A spectrophotometric approach based on the colorimetric reaction of phenol with the Folin–Ciocalteu reagent was used to quantify the total amount of polyphenols [40]. The findings are given in milligrams of gallic acid equivalent (GAE) for each gram of the sample's dry matter. The DPPH and FRAP techniques were used to quantify antioxidant activity. By using the process outlined by Brand-Williams et al. [41], the 2,2-diphenyl-2-picrylhydrazyl (DPPH) radical was reduced in a methanol solution as part of the DPPH method. The results are shown as millimoles of Trolox equivalent for each gram of sample dry matter. According to the method of Benzie and Strain [42], the FRAP technique comprises reducing the colorless complex of iron (III) tri-pyridyltriazine (Fe^{3+}-TPTZ) to the ferrous form (Fe^{2+}), resulting in a vivid blue color. The FRAP results are expressed in millimoles of $FeSO_4 \cdot 7H_2O$ per gram of dry matter in the sample. The extracts' chemical properties were evaluated in triplicate, and the findings are shown as mean values ± standard deviations.

2.2.5. Statistical Analysis and Data Modeling

Three parallel experiments were used to assess all the physical and chemical characteristics of the extracted materials. The Statistica 14.0 software package (TIBCO® Statistica, Palo Alto, CA, USA) was used to perform basic statistical analysis, including mean and standard deviation. The Spearman correlation matrix function in Statistica 14.0 was used to look at correlations between the extraction conditions and the samples' physical and chemical characteristics.

Utilizing a Box–Behnken design integrated into the Statistica 14.0 software program, the effects of four independent variables (extraction time (X_1), extraction temperature (X_2), solid-to-liquid ratio (X_3), and mixing speed (X_4)) were evaluated. The aqueous grape skin extracts were subjected to the simultaneous optimization of three chemical parameters (total phenolic content, TPC, DPPH antioxidant activity, and FRAP antioxidant activity) and two physical properties (conductivity and total dissolved solids— TDS), expressed as Y. Thirty experiments were conducted at random in accordance with the experimental design, and the effect of each variable was studied at three levels (−1, 0, and 1). Equations of second-order polynomials were used to fit the experimental data. Utilizing the Statistica 14.0 software (TIBCO® Statistica, Palo Alto, CA, USA), response surface modeling was

carried out. The suggested response surface models served as the basis for estimating the ideal extraction conditions.

3. Results

3.1. Aqueous Extracts from Grape Skin: Their Physical and Chemical Properties

In this study, two classical solid–liquid extraction processes were conducted. In the first experiment, biologically active components were extracted from ground grape pomace skin, while in the second experiment, extraction was performed using previously dried and ground grape pomace skin. Thirty trials were carried out in a variety of settings to guarantee the best extraction conditions. The produced extracts' physical characteristics were analyzed, and the findings are shown in Table 1. Upon analyzing the results, it was observed that the lowest pH value in the first experimental set was 3.94 for sample 6 (t = 27.5 min, T = 60 °C, S/L = 30 g/L, and rpm = 250 L/min), while the highest pH value was 4.15 for sample 20 (t = 40 min, T = 60 °C, S/L = 10 mg/L, and rpm = 500). Nonetheless, based on the other pH values identified it may be concluded that the extraction conditions had very little impact on the extracts' pH. The results indicate that the prior drying of grape pomace skin does not notably affect the pH value as the range of pH values falls between 3.93 and 4.14. This range is in line with the pH range (pH 3.4–5.8) for this kind of residue, which is frequently mentioned in the literature [23,43].

According to the obtained results for experimental set 1, the lowest values for electrical conductivity and total dissolved solids were measured in sample 7 (t = 27.5 min, T = 60 °C, S/L = 10 g/L, and rpm = 750 L/min), and the highest values in sample 17 (t = 27.5 min, T = 80 °C, S/L = 30 g/L, and rpm = 500 L/min), indicating that increasing the temperature and extracting a larger amount of sample increases both the total dissolved substance and the electrical conductivity. For experimental set 2, the highest values for TDS and S were also shown by sample 17 (t = 27.5 min, T = 80 °C, S/L = 30 g/L, and rpm = 500 L/min), and the lowest values by sample 20 (t = 40 min, T = 60 °C, S/L = 10 g/L, and rpm = 500 L/min), again indicating that at higher temperatures and larger amounts of sample, there is an increase in total dissolved matter and electrical conductivity. According to the work of Pinel et al. [44], increasing the temperature promotes extraction by improving the solubility of the substance. By comparing experiments 1 and 2, it can be concluded that experiment 2, in which a sample of dried and ground skin was used, shows higher TDS and electrical conductivity values because such a sample of grape pomace is exposed to a larger contact surface with the solvent than only ground grape pomace skin, which is evident from the obtained results.

At different temperatures, mixing speeds, extraction times, and solid-to-liquid ratios, the chemical properties of the extracts were examined: the total amount of polyphenols and the antioxidant activity of grape pomace extracts were measured according to the DPPH and FRAP methods. For experiment 1, the highest amount of polyphenols was observed in sample 15 (t = 27.5 min, T = 80 °C, S/L = 10 g/L, and rpm = 500 L/min), at 15.33 $mg_{GAE}/g_{d.m.}$, while the lowest value was in sample 16 (t = 27.5 min, T = 40 °C, S/L = 30 g/L, and rpm = 500 L/min) at 3.55 $mg_{GAE}/g_{d.m.}$, almost five times lower than in sample 15. A similar trend was noticed for extracts after experiment 2; the highest value of total polyphenols was measured in sample 24 (t = 27.5 min, T = 80 °C, S/L = 20 g/L, and rpm = 250 L/min) at 17.13 $mg_{GAE}/g_{d.m.}$, while the lowest value was in sample 25 (t = 27.5 min, T = 40 °C, S/L = 20 g/L, and rpm = 750 L/min) at 5.04 $mg_{GAE}/g_{d.m.}$. Moreover, the nature and polarity of the solvent, the methods used for isolation, the purity of the active ingredients, and the instrument employed to measure the antioxidant activity all affect the antioxidant activity of plant extracts [45]. When determining the antioxidant activity of extracts after experiment 1, the highest values for DPPH and FRAP were measured precisely in sample 15: DPPH = 0.0447 $mmol_{Trolox}/g_{d.m.}$ and FRAP = 0.0779 $mmol_{Trolox}/g_{d.m.}$, while the lowest values for DPPH were seen in sample 1 (DPPH = 0.0002 $mmol_{Trolox}/g_{d.m.}$) and for FRAP in sample 16 (FRAP = 0.0135 $mmol_{FeSO4\cdot7H2O}/g_{d.m.}$). Small deviations are visible with DPPH; however, if we look at samples 1 and 16, we see that the temperature

parameters and the solid-to-liquid ratio are the same in both cases, confirming that the extraction efficiency increases with increasing temperature, while other parameters are not significant. In the case of extracts prepared according to experiment 2, the highest values of DPPH and FRAP were measured in sample 24 (DPPH = 0.0611 $mmol_{Trolox}/g_{d.m.}$ and FRAP = 0.1256 $mmol_{FeSO4 \cdot 7H2O}/g_{d.m.}$), and the lowest values were recorded for sample 1 (t = 15 min, T = 40 °C, S/L = 20 g/L, and rpm = 500 L/min) for DPPH and sample 25 (t = 27.5 min, T = 40 °C, S/L = 20 g/L, and rpm = 750 L/min) for FRAP.

Table 1. Physical and chemical properties of the aqueous extracts from grape skin after experiment 1 (green shading) and experiment 2. X_1—extraction time, X_2—extraction temperature, X_3—solid–to-liquid ratio, X_4—mixing speed, S—conductivity, TDS—total dissolved solids, TPC—total polyphenol content, DPPH—antioxidant activity measured by the DPPH method, and FRAP—antioxidant activity measured by the FRAP method.

Exp.	X_1	X_2	X_3	X_4	pH	S (µS/cm)	TDS (mg/L)	TPC ($mg_{GAE}/g_{d.m.}$)	DPPH ($mmol_{Trolox}/g_{d.m.}$)	FRAP ($mmol_{FeSO4 \cdot 7H2O}/g_{d.m.}$)
1.	15	40	20	500	4.16 ± 0.06	188.20 ± 1.90	380.50 ± 0.71	4.82 ± 0.0001	0.0002 ± 0.0017	0.0168 ± 0.0018
					4.04 ± 0.01	370.50 ± 7.78	704.00 ± 8.49	7.27 ± 0.1754	0.0158 ± 0.0006	0.0349 ± 0.0022
2.	40	40	20	500	4.02 ± 0.03	167.70 ± 0.14	319.50 ± 17.68	5.23 ± 0.0002	0.0119 ± 0.0007	0.0186 ± 0.0081
					4.00 ± 0.01	431.50 ± 0.71	868.00 ± 1.41	5.84 ± 0.0877	0.0124 ± 0.0001	0.0276 ± 0.0025
3.	15	80	20	500	4.03 ± 0.03	156.8 ± 0.14	311.00 ± 1.41	9.11 ± 0.0005	0.0401 ± 0.0015	0.0412 ± 0.0075
					3.97 ± 0.01	368.50 ± 0.71	756.00 ± 8.49	14.71 ± 0.2631	0.0548 ± 0.0006	0.0985 ± 0.0021
4.	40	80	20	500	3.95 ± 0.02	257.00 ± 0.00	488.50 ± 21.92	9.90 ± 0.0007	0.0447 ± 0.0005	0.0399 ± 0.0199
					3.98 ± 0.01	397.00 ± 0.00	811.00 ± 2.83	15.70 ± 0.5262	0.0497 ± 0.0014	0.1032 ± 0.0022
5.	27.5	60	10	250	4.12 ± 0.01	102.70 ± 0.63	214.50 ± 4.95	7.87 ± 0.0004	0.0210 ± 0.0007	0.0244 ± 0.0241
					4.13 ± 0.03	229.00 ± 0.00	456.50 ± 0.71	10.57 ± 0.7600	0.0326 ± 0.0016	0.0442 ± 0.0193
6.	27.5	60	30	250	3.94 ± 0.00	211.50 ± 0.70	418.50 ± 4.95	3.96 ± 0.0001	0.0125 ± 0.0002	0.0186 ± 0.0059
					3.91 ± 0.01	416.00 ± 15.56	861.50 ± 6.36	7.41 ± 0.3508	0.0236 ± 0.0004	0.0470 ± 0.0029
7.	27.5	60	10	750	4.13 ± 0.04	97.75 ± 0.49	198.70 ± 0.71	8.43 ± 0.0011	0.0182 ± 0.0026	0.0295 ± 0.0018
					4.02 ± 0.04	238.5 ± 0.71	488.00 ± 9.89	13.17 ± 0.0000	0.0395 ± 0.0016	0.0739 ± 0.0082
8.	27.5	60	30	750	3.99 ± 0.01	216.00 ± 2.83	442.00 ± 1.41	5.67 ± 0.0006	0.0114 ± 0.0011	0.0236 ± 0.0004
					3.98 ± 0.02	380.5 ± 6.36	7850 ± 2.82	7.28 ± 0.2631	0.0212 ± 0.0001	0.0398 ± 0.0041
9.	27.5	60	20	500	4.01 ± 0.01	148.15 ± 1.06	286.50 ± 4.95	5.61 ± 0.0004	0.0162 ± 0.0015	0.0265 ± 0.0018
					3.93 ± 0.04	337.50 ± 0.71	664.50 ± 6.36	8.51 ± 0.0877	0.0229 ± 0.0025	0.0421 ± 0.0030
10.	15	60	20	250	3.97 ± 0.01	164.45 ± 0.35	330.00 ± 0.00	5.29 ± 0.0005	0.0146 ± 0.0005	0.0239 ± 0.0038
					3.99 ± 0.01	350.50 ± 10.61	724.00 ± 2.83	10.49 ± 0.0000	0.0330 ± 0.0025	0.0629 ± 0.0023
11.	40	60	20	250	4.04 ± 0.01	152.20 ± 0.28	305.50 ± 0.71	5.38 ± 0.0006	0.0041 ± 0.0002	0.0262 ± 0.0001
					3.98 ± 0.04	350.00 ± 0.00	659.50 ± 23.33	11.17 ± 0.0000	0.0363 ± 0.0003	0.0624 ± 0.0077
12.	15	60	20	750	4.07 ± 0.04	155.00 ± 0.85	293.50 ± 4.95	4.87 ± 0.0009	0.0030 ± 0.0012	0.0231 ± 0.0002
					4.02 ± 0.04	373.50 ± 0.71	757.00 ± 11.31	7.95 ± 0.0000	0.0178 ± 0.0008	0.0360 ± 0.0015
13.	40	60	20	750	4.07 ± 0.04	165.75 ± 0.77	304.00 ± 8.49	5.75 ± 0.0012	0.0055 ± 0.0008	0.0293 ± 0.0011
					4.03 ± 0.03	289.50 ± 7.78	615.00 ± 14.14	9.62 ± 0.0000	0.0269 ± 0.0005	0.0415 ± 0.0157
14.	27.5	40	10	500	4.14 ± 0.01	118.90 ± 0.85	216.20 ± 39.32	6.84 ± 0.0017	0.0062 ± 0.0013	0.0265 ± 0.0101
					4.07 ± 0.01	266.00 ± 1.41	538.50 ± 4.95	8.09 ± 0.0000	0.0185 ± 0.0013	0.0015 ± 0.0355
15.	27.5	80	10	500	4.00 ± 0.04	194.55 ± 0.91	392.50 ± 0.71	15.33 ± 0.0018	0.0447 ± 0.0007	0.0779 ± 0.0237
					4.11 ± 0.02	231.00 ± 0.00	465.50 ± 4.95	16.27 ± 0.0000	0.0556 ± 0.0000	0.0647 ± 0.0392
16.	27.5	40	30	500	4.02 ± 0.00	232.50 ± 7.77	485.00 ± 0.00	3.55 ± 0.0004	0.0019 ± 0.0006	0.0135 ± 0.0103
					3.97 ± 0.01	429.00 ± 1.41	896.50 ± 2.12	5.30 ± 0.0000	0.0124 ± 0.0007	0.0167 ± 0.0105
17.	27.5	80	30	500	4.00 ± 0.01	295.50 ± 0.70	585.50 ± 2.12	8.68 ± 0.0015	0.0407 ± 0.0183	0.0419 ± 0.0053
					3.96 ± 0.02	484.00 ± 1.41	971.50 ± 0.71	14.23 ± 0.0000	0.0431 ± 0.0003	0.0744 ± 0.0083
18.	27.5	60	20	500	4.02 ± 0.03	140.30 ± 0.42	282.50 ± 0.71	4.54 ± 0.0006	0.0098 ± 0.0000	0.0232 ± 0.0215
					4.08 ± 0.02	273.50 ± 6.37	572.50 ± 4.95	8.38 ± 0.0000	0.0227 ± 0.0003	0.0308 ± 0.0281
19.	15	60	10	500	4.11 ± 0.01	106.75 ± 0.91	202.50 ± 3.54	7.50 ± 0.0018	0.0069 ± 0.0013	0.0319 ± 0.0055
					4.14 ± 0.01	200.00 ± 0.00	365.50 ± 6.36	11.56 ± 0.0000	0.0298 ± 0.0039	0.0453 ± 0.0029
20.	40	60	10	500	4.15 ± 0.07	122.95 ± 2.47	204.00 ± 5.66	9.92 ± 0.0015	0.0152 ± 0.0017	0.0459 ± 0.0068
					4.11 ± 0.02	195.80 ± 0.35	391.50 ± 0.71	8.71 ± 0.0000	0.0289 ± 0.0016	0.0589 ± 0.0310
21.	15	60	30	500	4.05 ± 0.00	173.50 ± 1.41	351.50 ± 0.71	5.05 ± 0.0005	0.0064 ± 0.0006	0.0173 ± 0.0021
					4.03 ± 0.01	376.50 ± 0.71	741.00 ± 11.31	6.79 ± 0.4092	0.0201 ± 0.0008	0.0392 ± 0.0017
22.	40	60	30	500	3.99 ± 0.01	208.00 ± 0.00	414.00 ± 1.41	5.57 ± 0.0007	0.0133 ± 0.0043	0.0245 ± 0.0074
					4.05 ± 0.01	446.00 ± 7.07	504.00 ± 2.83	7.49 ± 0.0000	0.0198 ± 0.0004	0.0401 ± 0.0073
23.	27.5	40	20	250	4.00 ± 0.02	202.00 ± 2.82	410.00 ± 0.00	4.63 ± 0.0001	0.0037 ± 0.0003	0.0174 ± 0.0006
					3.99 ± 0.01	405.00 ± 5.66	784.50 ± 4.95	5.84 ± 0.3508	0.0172 ± 0.0010	0.0294 ± 0.0050
24.	27.5	80	20	250	4.06 ± 0.01	191.85 ± 0.92	391.00 ± 5.66	8.27 ± 0.0018	0.0229 ± 0.0023	0.0420 ± 0.0056
					4.00 ± 0.01	386.00 ± 1.41	765.00 ± 5.65	17.13 ± 0.0877	0.0611 ± 0.0110	0.1256 ± 0.0028

Table 1. *Cont.*

Exp.	X_1	X_2	X_3	X_4	pH	S (µS/cm)	TDS (mg/L)	TPC ($mg_{GAE}/g_{d.m.}$)	DPPH ($mmol_{Trolox}/g_{d.m.}$)	FRAP ($mmol_{FeSO4·7H2O}/g_{d.m.}$)
25.	27.5	40	20	750	4.12 ± 0.03	147.75 ± 4.31	295.50 ± 9.19	5.52 ± 0.0002	0.0067 ± 0.0056	0.0167 ± 0.0003
					4.02 ± 0.00	374.50 ± 0.71	755.00 ± 1.41	5.04 ± 0.5262	0.0140 ± 0.0001	0.0266 ± 0.0068
26.	27.5	80	20	750	4.08 ± 0.02	250.50 ± 0.71	509.50 ± 4.95	11.07 ± 0.0012	0.0427 ± 0.0025	0.0534 ± 0.0076
					4.05 ± 0.01	389.00 ± 1.41	766.00 ± 7.07	14.15 ± 0.5262	0.0399 ± 0.0003	0.0828 ± 0.0029
27.	27.5	60	20	500	4.04 ± 0.03	158.75 ± 0.49	319.50 ± 0.71	6.92 ± 0.0002	0.0124 ± 0.0008	0.0291 ± 0.0026
					4.06 ± 0.00	398.50 ± 2.12	812.50 ± 7.78	8.32 ± 0.0000	0.0233 ± 0.0005	0.0421 ± 0.0000
28.	27.5	60	20	500	3.98 ± 0.02	153.85 ± 0.92	311.00 ± 0.00	5.71 ± 0.0004	0.0138 ± 0.0005	0.0310 ± 0.0003
					4.09 ± 0.01	355.50 ± 4.95	734.00 ± 5.66	7.45 ± 0.0877	0.0180 ± 0.0009	0.0387 ± 0.0052
29.	27.5	60	20	500	3.98 ± 0.02	151.15 ± 0.92	261.00 ± 9.89	5.85 ± 0.0005	0.0151 ± 0.0051	0.0300 ± 0.0006
					3.90 ± 0.01	394.50 ± 0.71	783.00 ± 2.83	8.51 ± 0.6139	0.0274 ± 0.0012	0.0496 ± 0.0020
30.	27.5	60	20	500	4.00 ± 0.01	144.75 ± 0.78	292.50 ± 0.71	6.17 ± 0.0009	0.0002 ± 0.0017	0.0245 ± 0.0004
					3.98 ± 0.01	374.50 ± 0.71	741.50 ± 12.02	9.62 ± 0.0000	0.0248 ± 0.0009	0.0546 ± 0.0029

According to the obtained results, we can conclude that an increase in temperature favored the extraction, while the mixing speed had a negative effect on the extraction efficiency. This negative effect might be due to the possible retention of the sample on the walls of the glass, or at a rotation speed of 750 L/min, the sample might have been ejected from the solution, resulting in a reduced amount of sample being extracted. Multiple researchers suggest that raising the extraction temperature improves the substance's solubility, which in turn promotes the rate of extraction.

Also, it is important to point out that temperature significantly influenced the obtained results while the mixing speed and the extraction time remained constant. Benchaachoua et al. [46] conducted a study on the influence of different solvents on the extraction of phenolic compounds from thistle root extract. They discovered that the water–ethanol (50:50, *v*/*v*) solvent extract had the highest concentration of phenolic chemicals, measuring 17.22 $mgGAE/g_{d.m.}$. The water extract had a slightly lower concentration of phenolic compounds (16.38 $mgGAE/g_{d.m.}$), but the difference was not statistically significant ($p < 0.05$). Comparable outcomes were found in the above study, indicating that the effectiveness of the solvent's extraction process is dependent on the type of phenolic chemicals present in the plant. Although the water–ethanol solvent is appropriate for acquiring biologically active compounds with a variety of polarizations due to the relatively polar environment created by the addition of organic solvents to water, the application of water as an extraction solvent generates a highly polar surrounding that is acceptable for extracting strongly polarizing biologically active substances [47]. Valinger et al. [24], who conducted the extraction of polyphenols from olive leaves, obtained the highest concentration of polyphenols at 80 °C and the lowest value at 40 °C while the other parameters of mixing speed and extraction time remained the same. They also found the highest antioxidant activity using the DPPH and FRAP methods in the same samples with the highest polyphenol concentration. These outcomes agree with this study's conclusions. By comparing the chemical properties of extracts prepared in experiment 1 and experiment 2, it can be seen that slightly higher values were obtained in experiment 2, where a dried and ground sample was used, which contributed to a larger contact surface with the solvent itself, compared to the case of only ground samples in experiment 1, which resulted in better extraction. The obtained polyphenol concentration from the extraction process aligns with the findings in the existing literature. For instance, Libran et al. [48] reported an extraction efficiency of 5 $mg_{GAE}/g_{d.m.}$ from white grape skin. Similarly, Yammine et al. [49] documented an extraction efficiency of 3.07 $mg_{GAE}/g_{d.m.}$, and Gerardi et al. [50] reported a range of 1.2 to 3.07 $mg_{GAE}/g_{d.m.}$ for polyphenol extraction efficiency. It is worth noting that ethanol was employed as the extracting agent in all the aforementioned experiments. Comparing our results to those presented by Sokač Cvetnić et al. [38], it can be noticed that grape skin grinding and drying have a significant effect on extraction efficiency. The abovementioned authors reported a value of 8.38 $mg_{GAE}/g_{d.m.}$ under optimal process conditions.

Optimizing extraction time and temperature is crucial for lowering energy costs and achieving high compound recovery percentages. There is broad agreement among authors that raising the working temperature improves the solubility of chemicals, which in turn improves extraction efficiency. High temperatures do, nonetheless, have a beneficial influence on extraction yields; however, these variables are unable to be elevated continuously since temperatures above 80 °C may degrade polyphenols. [51]. Some studies have indicated that a temperature of 60 °C enhances phenol extraction from grapes [52]. Additionally, according to Pinelo et al. [44], contact time is not as significant when water is used as a solvent.

3.2. Relationships between Extraction Conditions and Physical and Chemical Properties of the Aqueous Extracts from Grape Skin

To elucidate the relationship between the physical and chemical properties of the prepared grape skin extracts, a correlation matrix was constructed. Tables 2 and 3 present the correlation coefficients between temperature, solid-to-liquid ratio, extraction time, mixing speed, pH, total dissolved solids (TDS), electrical conductivity, total polyphenol concentration, and antioxidant activity determined by both the DPPH and FRAP methods. Significant correlations are highlighted in bold.

For extracts from experiment 1, total polyphenols exhibited positive correlations with extraction time (r = 0.110), temperature (r = 0.681), and mixing speed (r = 0.127), while a negative correlation was observed with the solid-to-liquid ratio (r = −0.502). This trend was similarly observed for antioxidant activities determined by the DPPH and FRAP methods. Comparable findings were reported by Pinelo et al. [44], who discovered that temperature and solid-to-liquid ratio were crucial factors in maximizing extraction effectiveness. Notably, pH values showed a positive correlation solely with total polyphenols (r = 0.103), while TDS exhibited positive correlations with all variables, except pH. Additionally, extraction time and temperature displayed positive correlations with all chemical and physical characteristics, except pH, while the solid-to-liquid ratio exhibited negative correlations with all parameters, except TDS and electrical conductivity.

Table 2. Spearman correlation matrix of physical and chemical characteristics of grape pomace skin extracts prepared by the classical extraction procedure for experiment 1. Significant correlations are shown in bold.

	t	T	S/L	rpm	pH	TDS	S	TPC	DPPH	FRAP
t	**1**									
T	0.000	**1**								
S/L	0.000	0.000	**1**							
rpm	0.000	0.000	0.000	**1**						
pH	**−0.138**	**−0.166**	**−0.390**	**0.163**	**1**					
TDS	**0.147**	**0.331**	**0.678**	0.009	**−0.384**	**1**				
S	**0.091**	**0.313**	**0.694**	−0.014	**−0.367**	**0.989**	**1**			
TPC	**0.110**	**0.681**	**−0.502**	**0.127**	**0.103**	**0.116**	**0.094**	**1**		
DPPH	**0.122**	**0.754**	**−0.391**	**0.094**	−0.005	**0.196**	**0.166**	**0.946**	**1**	
FRAP	**0.095**	**0.824**	**−0.105**	0.035	**−0.199**	**0.439**	**0.417**	**0.820**	**0.799**	**1**

In the case of extracts from experiment 2, extraction time positively correlated with antioxidant activity measured by both the DPPH (r = 0.034) and FRAP (r = 0.010) methods, as well as with TDS (r = 0.049) and pH values (r = 0.056), while negatively correlating with electrical conductivity (r = −0.069) and total polyphenols (r = −0.004). Positive correlations were observed between extraction temperature and chemical characteristics (total polyphenols, DPPH, and FRAP), with negative correlations evident with physical

characteristics. Mixing speed (rpm) displayed negative correlations with all variables, except pH value. Furthermore, chemical characteristics (total polyphenols and antioxidant activity measured by both the FRAP and DPPH methods) exhibited positive correlations with each other and with temperature.

Table 3. Spearman correlation matrix of physical and chemical characteristics of grape pomace skin extracts prepared by the classical extraction procedure for experiment 2. Significant correlations are shown in bold.

	t	T	S/L	rpm	pH	TDS	S	TPC	DPPH	FRAP
t	**1**									
T	0.000	**1**								
S/L	0.000	0.000	**1**							
rpm	0.000	0.000	0.000	**1**						
pH	**0.056**	−0.012	**−0.641**	**0.100**	**1**					
TDS	**0.049**	**−0.093**	**0.832**	**−0.065**	**−0.709**	**1**				
S	**−0.069**	**−0.056**	**0.713**	−0.029	**−0.750**	**0.882**	**1**			
TPC	−0.004	**0.861**	**−0.312**	**−0.085**	**0.051**	**−0.259**	**−0.188**	**1**		
DPPH	0.034	**0.839**	**−0.063**	**−0.145**	**−0.138**	0.007	**0.051**	**0.873**	**1**	
FRAP	0.010	**0.858**	**−0.259**	**−0.178**	0.002	**−0.223**	**−0.149**	**0.970**	**0.905**	**1**

3.3. RSM Modeling and Optimization of the Grape Extraction Procedure

This investigation examined the effects of four process variables—temperature, time, mixing speed, and solid-to-liquid ratio—on extracts' chemical and physical characteristics, including total polyphenol content and antioxidant activity as measured by FRAP and DPPH assays, as well as their conductivity, total dissolved solids, and pH. To fit the model to the data, second-order polynomial equations were used in the course of this study.

The coefficients of determination (R^2) of the developed models ranged from 0.2709 to 0.9609 (see Table 4). The best agreement between the Response Surface Methodology (RSM) model and experimental data was observed for conductivity values in experimental set 1, while the lowest agreement was found for the pH value in experimental set 2. The R^2 values for total dissolved solids and electrical conductivity ranged from 0.9555 to 0.9609, indicating a very good fit of the model to the experimental data. For total polyphenols, an R^2 value of 0.8976 was obtained, while for antioxidant activity, the RSM-based models showed a high agreement with the experimental data, with R^2 = 0.9469 for DPPH and 0.8937 for FRAP.

Table 4. RSM models for the description of physical and chemical characteristics of grape pomace skin extracts prepared by the classical extraction procedure after experiment 1 (green shading) and experiment 2. Statistically significant coefficients are shown in bold.

Model Variable	RSM Equation	R^2	F-Value	*p*-Value
pH	$Y = \mathbf{4.091} - \mathbf{0.069}\cdot X_3$	0.2709	5.4624	0.0274
	$Y = \mathbf{4.027} - \mathbf{0.065}\cdot X_3$	0.4417	4.5495	0.0075
TDS	$Y = 153.597 + 10.740\cdot X_1 + \mathbf{30.133}\cdot X_2 + \mathbf{52.070}\cdot X_3 + 1.58\cdot X_4 - 4.293\cdot X_1^2 - \mathbf{46.784}\cdot X_2^2 - 3.901\cdot X_3^2 - 4.464\cdot X_4^2 + \mathbf{36.195}\cdot X_1X_2 + 5.49\cdot X_1X_3 + 9.071\cdot X_1X_4 - 3.163\cdot X_2X_3 + \mathbf{28.225}\cdot X_2X_4 + 2.35\cdot X_3X_4$	0.9555	19.9534	<0.0001
	$Y = 349.625 + 9.269\cdot X_1 - 12.541\cdot X_2 + \mathbf{95.401}\cdot X_3 - 10.907\cdot X_4 - 0.919\cdot X_1^2 + \mathbf{41.497}\cdot X_2^2 - \mathbf{29.575}\cdot X_3^2 - 5.442\cdot X_4^2 - 9.75\cdot X_1X_2 + 22.125\cdot X_1X_3 - 32.703\cdot X_1X_4 - 5\cdot X_2X_3 + 8.375\cdot X_2X_4 - 11.25\cdot X_3X_4$	0.8241	8.5362	0.0002

Table 4. *Cont.*

Model Variable	RSM Equation	R^2	F-Value	*p*-Value
S	$Y = 297.751 + 8.730 \cdot X_1 + \mathbf{59.533} \cdot X_2 + \mathbf{111.415} \cdot X_3 - 0.806 \cdot X_4 - 20.482 \cdot X_1^2 - \mathbf{98.472} \cdot X_2^2 - 11.961 \cdot X_3^2 - 15.837 \cdot X_4^2 + \mathbf{71.55} \cdot X_1 X_2 + 18.3 \cdot X_1 X_3 + 13.776 \cdot X_1 X_4 - 18.95 \cdot X_2 X_3 + \mathbf{58.25} \cdot X_2 X_4 + 9.825 \cdot X_3 X_4$	0.9609	22.8023	<0.0001
	$Y = 725.076 - 49.924 \cdot X_1 - 18.908 \cdot X_2 + \mathbf{161.733} \cdot X_3 - 9.918 \cdot X_4 - 99.578 \cdot X_1^2 + \mathbf{88.446} \cdot X_2^2 - \mathbf{119.1908} \cdot X_3^2 + 1.485 \cdot X_4^2 - 32.7 \cdot X_1 X_2 - 78.9 \cdot X_1 \cdot X_3 - 32.606 \cdot X_1 X_4 - 0.5 \cdot X_2 X_3 + 7.625 \cdot X_2 X_4 - 27 \cdot X_3 X_4$	0.9469	16.5601	<0.0001
TPC	$Y = 5.682 + 0.589 \cdot X_1 + \mathbf{2.663} \cdot X_2 - \mathbf{2.171} \cdot X_3 + 0.5407 \cdot X_4 + 0.145 \cdot X_1^2 + \mathbf{1.764} \cdot X_2^2 + 1.382 \cdot X_3^2 - 0.302 \cdot X_4^2 + 0.112 \cdot X_1 X_2 - 0.568 \cdot X_1 X_3 + 0.155 \cdot X_1 X_4 - 0.839 \cdot X_2 X_3 + 0.4778 \cdot X_2 X_3 + 0.287 \cdot X_3 X_4$	0.8976	8.1422	0.0003
	$Y = 8.640 + 0.071 \cdot X_1 + \mathbf{4.688} \cdot X_2 - 1.396 \cdot X_3 - 0.398 \cdot X_4 + 0.268 \cdot X_1^2 + \mathbf{1.845} \cdot X_2^2 + 0.136 \cdot X_3^2 + 0.622 \cdot X_4^2 + 0.725 \cdot X_1 X_2 + 1.066 \cdot X_1 X_3 + 0.284 \cdot X_1 X_4 + 0.186 \cdot X_2 X_3 - 0.542 \cdot X_2 X_4 - 0.682 \cdot X_3 X_4$	0.9043	8.7757	0.0002
DPPH	$Y = 0.027 + 0.002 \cdot X_1 + \mathbf{0.015} \cdot X_2 - 0.008 \cdot X_3 + 0.002 \cdot X_4 - 0.002 \cdot X_1^2 + \mathbf{0.007} \cdot X_2^2 + 0.003 \cdot X_3^2 - 0.002 \cdot X_4^2 - 0.001 \cdot X_1 X_2 - 0.002 \cdot X_1 X_3 + 0.002 \cdot X_1 X_4 - 0.006 \cdot X_2 X_3 + 0.003 \cdot X_2 X_4$	0.9469	16.5684	<0.0001
	$Y = 0.042 + 0.007 \cdot X_1 + \mathbf{0.034} \cdot X_2 - \mathbf{0.005} \cdot X_3 - \mathbf{0.005} \cdot X_4 + 0.012 \cdot X_1^2 + \mathbf{0.010} \cdot X_2^2 - 0.003 \cdot X_3^2 + 0.008 \cdot X_4^2 + 0.003 \cdot X_1 X_2 - 0.004 \cdot X_1 X_3 - 0.002 \cdot X_1 X_4 - 0.001 \cdot X_2 X_3 - 0.009 \cdot X_2 X_4 - 0.009 \cdot X_3 X_4$	0.9455	16.1230	<0.0001
FRAP	$Y = 0.014 + 0.002 \cdot X_1 + \mathbf{0.016} \cdot X_2 - \mathbf{0.003} \cdot X_3 + 0.001 \cdot X_4 - 0.004 \cdot X_1^2 + \mathbf{0.012} \cdot X_2^2 + \mathbf{0.002} \cdot X_3^2 - 0.003 \cdot X_4^2 - 0.002 \cdot X_1 X_2 - 0.0004 \cdot X_1 X_3 + 0.002 \cdot X_1 X_4 + 0.0001 \cdot X_2 X_3 + 0.004 \cdot X_2 X_4 + 0.0004 \cdot X_3 X_4$	0.8937	7.8000	0.0003
	$Y = 0.023 + 0.001 \cdot X_1 + \mathbf{0.018} \cdot X_2 - \mathbf{0.0058} \cdot X_3 - 0.003 \cdot X_4 + 0.002 \cdot X_1^2 + 0.007 \cdot X_2^2 + \mathbf{0.001} \cdot X_3^2 + 0.003 \cdot X_4^2 - 0.001 \cdot X_1 X_2 + 0.0002 \cdot X_1 X_3 + 0.001 \cdot X_1 X_4 - \mathbf{0.002} \cdot X_2 X_3 - 0.004 \cdot X_2 X_4 - 0.002 \cdot X_3 X_4$	0.9584	21.3800	<0.0001

Based on the F-values and *p*-values ($p < 0.05$), all models were found to be significant. Le Man et al. [53] stated that if a model shows a satisfactory fit between the experimental and predicted values and the coefficient of determination is greater than 0.75, it can be deemed relevant. Furthermore, as proposed by Teng et al. [54], smaller *p*-values and greater coefficients of regression for any given model component indicate a more significant impact on the variable under examination. The acquired values show that, within the examined range of variables, the suggested models are reliable.

Based on the developed Response Surface Methodology (RSM) models, extraction temperature and solid-to-liquid ratio are shown to be significant factors affecting the total polyphenol content and antioxidant activity measured by both the DPPH and FRAP methods. The beneficial impact of extraction temperature on the yield of polyphenol extraction has been highlighted by numerous authors [55–58]. In traditional extraction methods, the highest polyphenol yield is achieved within the temperature range of 60–80 °C, whereas the yield tends to decrease at temperatures exceeding 80 °C [59]. Furthermore, the solid-to-liquid ratio has been identified as a significant factor influencing polyphenol yield [38]. The relationships between these variables are graphically presented in Figure 2.

Based on the desirability profiles that were obtained from the RSM-projected values, the extraction conditions were optimized for the chemical characteristics of the extracts. The desirability scale was used, which ranges from 0 (very unpleasant) to 1. According to the optimization matrix design, the following circumstances must be met for the grape skin extract to have its ideal physical and chemical properties: (i) for experiment 1, extraction time (t) = 15 min, temperature (T) = 80 °C, solid-to-liquid ratio (S/L) = 10 g/L, and mixing speed (rpm) = 500 1/min and (ii) for experiment 2, extraction time (t) = 15 min, temperature (T) = 80 °C, solid-to-liquid ratio (S/L) = 10 g/L, and mixing speed (rpm)

= 375 1/min. The models were evaluated in a randomized study using predetermined optimal process settings, showing a satisfactory match between the model's estimated data and the experimental results, as shown in Table 5.

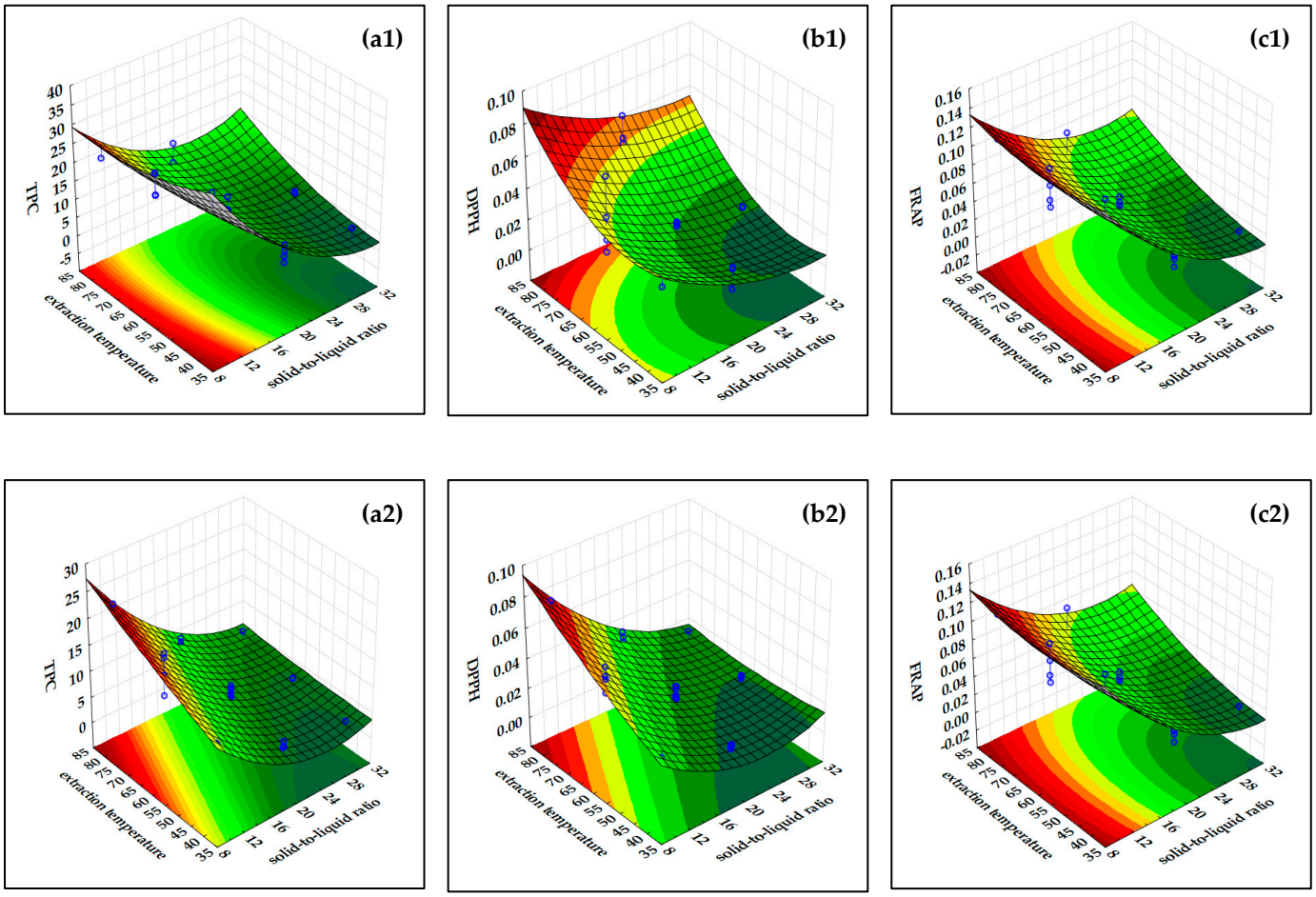

Figure 2. RSM models for the description of the chemical characteristics of grape pomace skin extracts prepared by the classical extraction procedure after experiment 1 and experiment 2. (**a**) Total polyphenol content, (**b**) antioxidant activity measured by the DPPH method, and (**c**) antioxidant activity measured by the FRAP method.

Table 5. Optimal extraction conditions and differences between the experimental data and model-predicted data under optimal conditions.

Model Output		Optimal Extraction Conditions	RMSE-Predicted Value of Output Variable	Experimental Value of Output Variable
Set 1	TPC	t = 15 min	26.6182	26.1284 ± 0.1287
	DPPH	T = 80 °C	0.0685	0.0601 ± 0.0011
	FRAP	S/L = 10 g/L rpm = 500 1/min	0.1210	0.1157 ± 0.0224
Set 2	TPC	t = 15 min	25.2930	25.1024 ± 0.0585
	DPPH	T = 80 °C	0.0831	0.0795 ± 0.0135
	FRAP	S/L = 10 g/L rpm = 375 1/min	0.0427	0.0440 ± 0.0022

4. Conclusions

The measured pH values of the extracts in both experiments did not differ much regarding the extraction conditions, and the obtained values corresponded to the pH range

of grape pomace that is often mentioned in the literature (3.4–5.8). By increasing the temperature and extracting a larger amount of sample, TDS and electrical conductivity increased in both experiments, and the correlation between them was confirmed because a significant part of the dissolved substances are ions that conduct electricity. Higher values were obtained in experiment 2 because such a sample was exposed to a larger contact surface with the solvent, and the removal of water from the sample improved the extraction efficiency. For both the first and second experiments, the most suitable physical and chemical characteristics of the grape skin extract were achieved under specified parameters determined by the optimization matrix architecture. For experiment 1, the optimal conditions were determined as follows: extraction time (t) = 15 min, temperature (T) = 80 °C, solid-to-liquid ratio (S/L) = 10 g/L, and mixing speed (rpm) = 500 1/min. Similarly, for experiment 2, the optimal conditions were as follows: extraction time (t) = 15 min, temperature (T) = 80 °C, solid-to-liquid ratio (S/L) = 10 g/L, and mixing speed (rpm) = 375 1/min. These findings demonstrate the effectiveness of the optimization process in identifying precise extraction conditions that yield optimal chemical properties in grape skin extracts. The presented results contribute to the valorization of grape skin as grape skin represents a valuable source of polyphenols with diverse biological activities. They are of interest in both the food and pharmaceutical industries and in scientific research exploring their health-promoting properties.

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