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Optimization of Process Variables for the Sustainable Extraction of Phenolic Compounds from Chicory and Fennel By-Products

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Abstract: The production of minimally processed vegetables generates large amounts of by-products whose concentrations in bioactive compounds is comparable to those of the edible part. The aim of this work was the optimization of sustainable processes for the extraction of phenolic compounds from chicory and fennel by-products using water as solvent. The results were compared with those obtained through a conventional extraction performed with a 70% ethanol aqueous solution as extraction solvent. The ultrasound-assisted extraction (UAE) and microwave-assisted extractions (MAE) were established by developing two Box–Behnken designs, respectively, a four-factor, three-level design and a three-factor, three-level design. A quadratic polynomial model was useful in optimizing both the ultrasonic (R^2 0.8473 for chicory and R^2 0.9208 for fennel) and microwave (R^2 0.9145 for chicory and R^2 0.7836 for fennel) extraction of bioactive compounds as well as the antioxidant activity of extract (R^2 0.8638 for chicory and R^2 0.9238 for fennel treated with ultrasounds; R^2 0.9796 for chicory and R^2 0.7486 for fennel submitted to MAE). The UAE conditions able to maximize the total phenolic concentrations were: 10 g/100 mL, 55 °C, t: 60 min, 72 W for chicory (9.07 mg gallic acid/g dm) and 15 g/100 mL, 45 °C, t: 40 min, 120 W for fennel (6.64 mg gallic acid/g dm). Concerning MAE, the highest phenolic concentrations were obtained applying 7.5 g/100 mL; 2 min; 350 W for chicory (8.23 mg gallic acid/g dm); 7.5 g/100 mL; 3 min; 160 W for fennel (6.73 mg gallic acid/g dm). Compared to conventional solvent extraction, UAE and MAE allowed the obtainment of (a) chicory extracts richer in phenolic compounds (+48% and +34%, respectively), in less time (4-fold and 90-fold reduction, respectively) and (b) fennel, extracts with slightly lower amount of phenolics (−11.7% and −10.5%, respectively) but halving the extraction time (UAE) or reducing it to 60-fold (MAE).

Keywords: circular economy; microwave-assisted extraction; phenolic compounds; sustainability; ultrasound-assisted extraction; vegetable by-products

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1. Introduction

In recent decades, the industry of minimally processed vegetables has grown exponentially worldwide. By-products of horticultural commodities significantly contribute to the waste produced by the fruit and vegetable processing industry, which in turn has been demonstrated to be the largest waste emitter into the environment, followed by the household waste generation [1]. Fruits and vegetables generate on average around 25–30% of waste (with peaks of over 50%) that is not further used despite its high contents in several classes of bioactive compounds that can be higher in by-products than in the final products. To better understand the scale of the waste problem, it is appropriate to provide some numerical data concerning specific products. Fruit and vegetable processing generates the following percentages of final products and by-products, respectively: sliced apples (89 and 10%); peeled mandarins (84 and 16%); diced papaya (53 and 47%); pineapples (48 and 52%); mango (58 and 42%); artichoke (34 and 66%); asparagus (50 and 50%); onion

(83 and 17%); tomato (80 and 20%) [2,3]. Hence, giving rise to the idea of recovering the bioactive compounds they trap, for example, through the modification of existing microwave drying system in order to both dry vegetables, such as ginger and onions, and, at the same time, collect the vapours containing bioactive components [4], or, in the case of wastewater from edible oil industry, their use to produce biomass, biofertilizers, biopesticides, biofuel, and bioplastics [5].

Chicory and fennel are among the most important vegetables marketed both as fresh and minimally processed products alone (this is the case with chicory) or as an ingredient in salads (fennel). Common chicory (*Cichorium intybus* L.) is an herbaceous plant of the Asteraceae family, typical of the Mediterranean region but now widely spread in other temperate and semi-arid areas (mid-Asia, northern Africa, eastern USA, Australia), both as a cultivated and wild plant. Chicory has been largely used in animal feed (the bagasse obtained after inulin extraction from roots), in the food industry (as ingredient for salad, for tea blends, as alternative to the more expensive coffee) but nowadays, there is an increasing interest for the extraction of functional compounds present in chicory, such as inulin, oligofructose and sesquiterpene lactones [6]. The interest towards chicory is not exclusively linked to its use as food and food supplement but also to it being a promising source of biologically active substances, such as hydroxycinnamic acids, coumarins and flavonoids, mainly distributed in the aboveground part of the plant, which act as effective immune-correcting agents [7]. Green chicory leaf extract is known to exert in vitro anti-inflammatory effects [8] and preparations obtained from chicory leaves, flowers, and roots have been employed for centuries to treat a great number of diseases in the traditional medicine of several Mediterranean and Asian countries [9]. Methanolic extracts of the spontaneous Romanian chicory species have demonstrated cardio-protective effects on myocardial ischemia and nephroprotection on renal failure in rats [10]. Ethanolic and methanolic extracts of chicory plant have demonstrated cytotoxic activities against cell line MCF-7 and AML, and such activity was related to the antioxidant activity and phenolic content of extracts [11]. According to the authors of that study, extracts can be used to protect or treat cancer cells. Enzyme-treated chicory roots also supplied extracts able to inhibit skin pathogen development in cosmetic formulas submitted to a challenge test [12]. Furthermore, chicory extracts are generally regarded as safe (GRAS) by the FDA and are included in the Everything Added to Food (EAFUS) list [13]. Fennel (*Foeniculum vulgare*) belongs to the Apiaceae/Umbelliferae family and is native to the Mediterranean and Asia Minor areas although the main producing countries are currently India, China, Indonesia, Egypt, and Pakistan. Fennel by-products are known as good sources of polyphenols having anti-inflammatory, antioxidant, immunomodulatory and apoptotic properties [14]. Malin et al. [15] highlighted only a weak antimicrobial effect of fennel seed extracts exerted against *Pseudomonas fragi*, *Shewanella putrefaciens*, and *Campylobacter jejuni.* Salami et al. [16] observed that the flavonoid and phenolic acid contents of fennel are strongly affected by geographical origin, thus influencing their antioxidant, antibacterial, and antiglycation properties. Furthermore, a study by Crescenzi et al. [17] highlighted that it is possible to discriminate the different plant parts through a metabolomic analysis since bulb is rich in dicaffeoyl quinic acid, while lusitanicoside and oxylipin trihydroxy-octadecadienoic acid II abound in leaves, and the stems contain oxylipin trihydroxy-octadecaeoic acid II.

Since the generation of increasing amounts of waste is compromising the environmental sustainability of food production, the full utilization of fruits and vegetables is both a duty and an opportunity for all those companies intending to implement low-waste technology in their agribusiness [1]. This result can be achieved through the extraction of bioactive compounds and natural food additives from waste and by-products, provided that the extraction processes are themselves sustainable [18]. According to Chemat et al. [19], a green extraction process must "reduce energy consumption, allow use of alternative solvents and renewable natural products, and ensure a safe and high quality extract/product". The design of green and sustainable extraction techniques is currently a hot research topic aiming to: reduce the consumption of petrochemical solvents, preferring bio-solvents, water, and

solvent-free techniques; reduce energy consumption and time by intensifying the extraction efficiency or recovering the same energy liberated during the extraction steps; produce extracts free from contaminants harmful for living creatures and the environment [19]. Several studies have been performed on the green extraction of phenolic compounds from chicory and fennel. Among the most recent, Cova et al. [20] applied UAE, MAE, and their combination using a hydroalcoholic solution or water alone (also sub-critical) to extract phenolic compounds from chicory. They found that MAE performed with sub-critical water, and MAE/UAE combinations carried out with an ethanol solution allowed the recovery of up to ~3 g of gallic acid equivalents per kg of fresh material in 15 min against the 240 min of conventional extraction. Pradal et al. [21] applied a Box–Wilson procedure (central composite design) for multi-criteria optimization of UAE of polyphenols from chicory and found that the targeted total phenolic yield (7.23 mg/g dm) was obtained under the following extraction conditions: 9.2 min, 60 °C, 37.5% of ethanol in the solvent, and ultrasound power of 100 W. Urango et al. [22] evaluated the impact of the combination of acoustic energy from 100 to 400 W with heat processing from 40 to 60 °C on the extraction of phenolic compounds from fennel. The highest yields (3.67 ± 0.07 mg/g dm) were obtained applying a power of 300 W at 60 °C, and using an ethanol/solid ratio of 10.

Given the huge amount of waste generated by the minimally processed vegetables industry and the growing importance of making food supply chains sustainable, our work was aimed to develop and optimize low environmental impact processes for the extraction of phenolic compounds from chicory and fennel by-products. Considering that the targeted result was the overall optimization of sustainable systems for the extraction of phenolic compounds, the highlights able to differentiate this work from other already published studies include the simultaneous presence of the following elements: the use of ultrasounds and microwaves to reduce treatment times; the total replacement of organic solvents with water; the application of the Box–Behnken design (four factors, three levels for ultrasound-assisted extraction; three factors, three levels for microwave-assisted extraction) in order to establish the number of trials and the combinations of process variables to test; the analysis of phenolic compounds and antioxidant activity; the use of response surface methodology as a method to optimize the extraction conditions; and, finally, the obtainment of aqueous extracts having phenolic concentrations comparable with those obtained by applying solvent extraction systems for considerably longer times.

2. Materials and Methods

2.1. By-Products and Pre-Treatments

Chicory and fennel by-products were collected from producers of minimally processed vegetables. Chicory by-products included external leaves, while those of fennel were represented by the outer leaves of the basal stems and leaves. The collected materials were washed under running tap water to remove traces of soil and foreign matter and were cut into regular pieces (10 ± 1 cm long for stems and external leaves; strips 1.0 ± 0.3 cm wide and 10 ± 1 cm long for the outer parts of fennel bulb) to prevent the excessive loss of cell juices and extensive oxidation, which would have occurred as a result of fine shredding. The pieces were blanched in water (solid–water ratio 1:6 w/w) at 90 ± 1 °C per 2 min to inactivate peroxidase and immediately cooled in cold water. The blanched by-products were then dried at 20 °C for 20 ± 4 h through a forced-air-drying system (until a final moisture of 1.85 ± 0.19% for chicory and 2.76 ± 0.26% for fennel was reached) to increase the extraction efficiency. The dried by-products were ground for 30 s with a blade mill (particle size distribution around 500 µm), taking care to keep the temperature below 30 °C, sealed in aluminium bags and stored at −20 °C until use.

2.2. Conventional Solvent Extraction

In order to compare the extraction efficiency of ultrasound- and microwave-assisted extractions with that of conventional extraction, phenolic compounds were extracted from the vegetable matrices using a 70% ethanol aqueous solution as extraction solvent

(solid–solvent ratio, 1:10 w/v) at two different temperatures (45 and 60 °C) for 30, 60, 90, 120 and 180 min. Since the temperatures proposed in the literature for phenolic extraction range from room temperature to 140 °C [23,24], the experimental conditions were selected considering that solubility and diffusion of phenolics increase with the increase in temperature but overheating could be responsible for their decomposition. To increase the contact surface between powdered by-products and solvent, an orbital shaker at a frequency of 200 rpm was used.

2.3. Ultrasound-Assisted Extraction

The UAE was developed according to a 4-factor, 3-level Box–Behnken design, and the response surface methodology was used to analyse the relationship between the individual and interactive effects of the extraction parameters and the dependent variables. Water was used as solvent. The four independent variables were coded at three levels (−1, 0, +1). The impacts of the solid–water ratio (5, 10, 15 g/100 mL), extraction temperature (35, 45, 55 °C), sonication time (20, 40, 60 min), and power (24, 72, 120 W) on total phenolic content, antioxidant activity, and individual phenolics were studied. The experimental design consisted of 27 total runs including 3 central points.

The extractions were performed in 500 mL Pyrex bottles put in a digital Ultrasonic Processor with 1 transducer (model DU-32 ArgoLab, Carpi, Italy), at a frequency of 40 KHz. Due to the variation in cavitation activity at different locations in the ultrasonic bath [25] and in order to standardize the extraction conditions, UAE was performed by placing the Pyrex bottle containing the sample precisely in the centre of the ultrasonic bath.

2.4. Microwave-Assisted Extraction

To investigate the relationship between the individual and interactive effects of the extraction parameters and the dependent variables measured, a 3-factor, 3-level BBD was applied, while RSM was used to optimize the extraction process. The three independent variables were coded at three levels (−1, 0, +1). Water was used as solvent. The impacts of the solid–water ratio (2.5, 5. 7.5 g/100 mL), treatment time (1, 2, 3 min), and power 90, 160, 350 W) on total phenolic content, antioxidant activity, and individual phenolics were studied. The design consisted of 15 total runs (3 central points included). The extractions were carried out in in 500 mL Pyrex bottles put in a microwave oven (model MWD 246, Whirlpool, Pero, Italy).

2.5. Analyses of the Extracts

The obtained extracts were cooled at 20 ± 2 °C and centrifuged for 10 min at 10,000 rpm (Thermo Scientific IEC CL31R Multispeed Laboratory centrifuge, Spinea, Italy). The supernatants were recovered, filtered through PVDF (polyvinylidene difluoride) membrane filters (45 µm) to eliminate any solid particles that could affect the results of the subsequent spectrophotometric and chromatographic analyses. The filtered supernatants were stored at temperatures below −18 °C until analysis.

The TPC was determined using the Folin–Ciocalteu method [26]. Briefly, 125 µL of previously diluted extract (1:5) was added to 500 µL of distilled water and 125 µL of FC reagent. After 5 min, 1250 µL of Na_2CO_3 (70 g/L) was added and the final volume was adjusted to 3000 µL with distilled water. The absorbance was measured at 760 nm, and results were expressed as mg of gallic acid/g of dry matter.

The DPPH radical scavenging activity was measured according to the method of Picinelli Lobo et al. [27] with some modifications. Briefly, 100 µL of each extract was added to 3900 µL of DPPH solution (40 mg/L) in methanol, and placed in the dark. A blank was prepared by adding 100 µL of distilled water to 3900 µL of DPPH. The absorbance of extracts and blank was measured at 515 nm after 90 min. The results of antioxidant activity were expressed as mg of Trolox per g of dry matter. Quantification was performed using a calibration curve prepared with increasing concentrations of Trolox.

The phenolic profiles of the extracts obtained applying for each technique the conditions able to maximize the TPC were analysed by high-pressure liquid chromatography according to Aliakbarian et al. [28]. The HPLC system was equipped with a diode array detector (Agilent 1100 Liquid Chromatograph, Santa Clara, CA, USA) and a 100 × 4.6 mm × 3 µm RP-C18 Gemini column (Phenomenex, Aschaffenburg, Germany). Separation was achieved using the following linear gradient of two solvents, Solvent A (1.0% acetic acid in water v/v) and Solvent B (50% methanol, 50% acetonitrile, v/v) at 30° C with a flow rate of 1 mL/min: from 5% to 25% B in 20 min; from 25% to 30% B in 5 min; from 30% to 40% B in 10 min; from 40% to 48% B in 5 min; from 48% to 60% B in 10 min, followed by returning to the initial conditions in 5 min and column equilibration (5 min). The injection volume was 100 µL. The compounds were identified on the basis of their retention times and comparing their spectra with those of standard compounds. The phenolic compounds were quantified at two wavelengths: 280 nm (gallic acid, 4-hydroxybenzoic acid, vanillic acid, caffeic acid, syringic acid, chlorogenic acid, ferulic acid, rosmarinic acid, epicatechin gallate, rutin, resveratrol, quercetin and kaempferol) and 320 nm (catechin, epicatechin, epigallocatechin, p-coumaric acid sinapic acid). Quantification was obtained by comparing the sample peak areas with those of standard curves. Data were expressed as mg/g dry matter.

2.6. Statistical Analysis

Each extraction trial was carried out in duplicate and analyses were repeated three times on each extract. The experimental results were expressed as means ± standard deviation of 6 data (n = 2 × 3), calculated using Excel software V. 14.0.0 for Mac. ANOVA, and LSD tests were applied to determine any significant differences ($p < 0.05$). Regarding UAE and MAE, the response variables were fitted to the following second order polynomial model:

$$Y = \beta_0 + \sum_{i=1}^{k} \beta_i X_i + \sum_{i=1}^{k} \beta_{ii} X_{ii}^2 + \sum_{i}^{k-1} \sum_{j}^{k} \beta_{ij} X_i X_j \quad (1)$$

where Y is the response; β_0 is constant; β_i are the linear coefficients; β_{ii} are the quadratic coefficients; and β_{ij} are the interactive coefficients. ANOVA was used to evaluate the quality of the fitted model and to individuate the significant factors (p-value < 0.05), while the overall predictive capability of the model was evaluated by the coefficient of determination (R^2). Response surface plots were generated using Statistica 7.0 (Statsoft Inc., New York, NY, USA).

3. Results and Discussion

3.1. Results of Conventional Solvent Extraction

Table 1 reports the TPC and antioxidant activity values of extracts corresponding to the eight temperature combinations and also the single effects of the two variables. For each time of treatment, the increase in temperature from 45 to 60 °C allowed to double the TPC of chicory extracts, while, in the case of fennel, the TPC doubled, tripled, or quadrupled. The highest TPCs were determined in chicory extracts treated at 60 °C for 180 min (6.14 ± 0.25 mg gallic acid/g dm) and in fennel extracts treated at 60 °C for 90 min (7.52 ± 0.85 mg gallic acid/g dm). Regarding the antioxidant activity of chicory, the highest values (around 0.0280 mmol Trolox/g dm) were observed in extracts obtained at 60 °C independent of the treatment time. The highest antioxidant activity of fennel extracts (0.0281 ± 0.0001 mmol Trolox/g dm) was obtained with treatment performed at 60 °C for 30 min, and also, in this case, a slight but statistically significant decrease was registered at longer treatment times. This means that in fennel, by prolonging the treatment beyond the optimal time, a slight but significant degradation of the phenolic fraction occurred. These results are in agreement with the literature; increases in temperature may favour the diffusion and improve the solubilisation of the phenolic compounds, thus increasing the extraction yield [29]; however, the adverse effects of increasing the time of treatment observed in some vegetable matrices can be attributed to the degradation, oxidation, or

polymerization of phenolic compounds and the generation of complexes with proteins and carbohydrates [30,31].

Table 1. Total phenolic content (mg gallic acid/g dm) and antioxidant activity (mmol Trolox/g dm) of extracts obtained through conventional extraction: single and interactive effects of temperature and time of treatment.

Extraction Conditions	Chicory By-Products		Fennel By-Products	
	TPC	AA	TPC	AA
Interactive effect of temperature and time of treatment				
T = 45 °C; t = 30 min	2.35 ± 0.09 ^{a}	0.0067 ± 0.0005 ^{a}	1.49 ± 0.16 ^{ab}	0.0051 ± 0.0001 ^{a}
T = 45 °C; t = 60 min	2.99 ± 0.21 ^{c}	0.0085 ± 0.0004 ^{b}	1.39 ± 0.15 ^{a}	0.0054 ± 0.0000 ^{a}
T = 45 °C; t = 90 min	3.93 ± 0.25 ^{d}	0.0124 ± 0.0010 ^{b}	2.09 ± 0.12 ^{b}	0.0074 ± 0.0004 ^{b}
T = 45 °C; t = 120 min	2.54 ± 0.16 ^{ab}	0.0090 ± 0.0006 ^{a}	2.78 ± 0.32 ^{c}	0.0095 ± 0.0005 ^{c}
T = 45 °C; t = 180 min	2.73 ± 0.23 ^{bc}	0.0126 ± 0.0002 ^{b}	2.85 ± 0.44 ^{c}	0.0108 ± 0.0010 ^{d}
T = 60 °C; t = 30 min	5.64 ± 0.33 ^{f}	0.0281 ± 0.0001 ^{c}	5.76 ± 0.13 ^{d}	0.0282 ± 0.0002 ^{f}
T = 60 °C; t = 60 min	4.93 ± 0.16 ^{e}	0.0281 ± 0.0000 ^{c}	6.93 ± 0.06 ^{ef}	0.0277 ± 0.0000 ^{e}
T = 60 °C; t = 90 min	5.77 ± 0.23 ^{fg}	0.0277 ± 0.0004 ^{c}	7.52 ± 0.85 ^{f}	0.0277 ± 0.0000 ^{e}
T = 60 °C; t = 120 min	5.56 ± 0.26 ^{f}	0.0281 ± 0.0000 ^{c}	6.71 ± 0.57 ^{e}	0.0274 ± 0.0000 ^{e}
T = 60 °C; t = 180 min	6.14 ± 0.25 ^{g}	0.0280 ± 0.0000 ^{c}	6.29 ± 0.30 ^{de}	0.0275 ± 0.0000 ^{e}
Significance	*	*	*	*
Single effect of temperature				
T = 45 °C	2.91 ^{a}	0.0099 ^{a}	2.12 ^{a}	0.0076 ^{a}
T = 60 °C	5.61 ^{b}	0.0280 ^{b}	6.64 ^{b}	0.0277 ^{b}
Significance	*	*	*	*
Single effect of time				
t = 30 min	3.99 ^{a}	0.0174 ^{a}	3.63 ^{a}	0.0167 ^{a}
t = 60 min	3.96 ^{a}	0.0183 ^{ab}	4.16 ^{b}	0.0165 ^{a}
t = 90 min	4.85 ^{c}	0.01996 ^{b}	4.80 ^{c}	0.0175 ^{b}
t = 120 min	4.05 ^{a}	0.01856 ^{ab}	4.75 ^{c}	0.0185 ^{c}
t = 180 min	4.44 ^{b}	0.0203 ^{b}	4.57 ^{bc}	0.0191 ^{d}
Significance	*	*	*	*

In columns, different superscript letters indicate significant differences ($p < 0.05$); * statistically significant at $p < 0.05$.

In agreement with the findings of Akowuah et al. and Hernández-Carranza et al. [32,33], strong correlations between phenolic content and antioxidant activity were observed for both the matrices (Equation (2), chicory; Equation (3), fennel):

$$AA = 0.0056TPC - 0.004 \quad R = 0.904 \tag{2}$$

$$AA = 0.0043TPC - 0.001 \quad R = 0.981 \tag{3}$$

3.2. Results of Ultrasound-Assisted Extraction

The TPC values obtained by applying the four-factor, three-level BBD are reported in Table 2. The total phenolic contents of chicory extracts were in the range of 2.15–9.07 mg gallic acid/g dm, and the extraction conditions that allowed the maximization of this index were the following: solid–water ratio = 10 g/100 mL; T = 55 °C; t = 60 min; power = 72 W. The total phenolic contents of fennel extracts were in the range of 2.13–6.64 mg gallic acid/g dm, and the highest values were obtained in the following conditions: solid–water ratio = 15 g/100 mL; T = 45 °C; t = 40 min; power = 120 W. For both by-products, the amounts of phenolic compounds extracted were higher than those obtained by other researchers (7.23 and 3.67 mg gallic acid/g dm, respectively) in shorter times but using ethanol or ethanol aqueous solutions as extraction solvents [10,11]. This is an important result since the research of Vauchel et al. [34] highlighted that ethanol use as solvent is a hotspot, leading to an important negative effect on environmental loads determined by the UAE of polyphenols from chicory grounds.

Table 2. Development of the Box–Behnken experimental design for ultrasound-assisted extraction: experimental results (observed) and values predicted by the models for total phenolic content and antioxidant activity; analyses of variance for linear, quadratic, and interactive effects of the independent variables and the determination coefficients of the models.

Extraction Conditions				Total Phenolic Content (mg Gallic Acid/g gm)						Antioxidant Activity (mmol Trolox/g dm)					
				Chicory By-Product Extracts			Fennel By-Product Extracts			Chicory By-Product Extracts			Fennel By-Product Extracts		
Solid/Water (g/100 mL)	T (°C)	t (min)	Power (W)	Observed	Predicted	%var.	Observed	Predicted	%var.	Observed	Predicted	%var.	Observed	Predicted	%var.
10	35	40	120	5.25 ± 0.08	5.48	4.40	4.59 ± 0.02	4.10	−10.65	0.0203 ± 0.0006	0.0181	−10.85	0.0268 ± 0.0000	0.0310	15.50
10	45	60	24	6.21 ± 0.28	7.06	13.72	5.41 ± 0.24	4.80	−11.30	0.0202 ± 0.0002	0.0189	−6.20	0.0293 ± 7.8 × 10^{-5}	0.0330	12.74
15	35	40	72	7.17 ± 0.00	6.48	−9.56	5.75 ± 0.11	5.86	1.83	0.0162 ± 0.0002	0.0143	−11.95	0.0198 ± 2 × 10^{-5}	0.0233	17.71
5	45	40	24	4.18 ± 1.12	4.14	−0.96	5.00 ± 0.16	4.33	−13.39	0.0312 ± 0.0054	0.0308	−1.23	0.0534 ± 0.0000	0.0512	−4.06
5	45	20	72	3.60 ± 0.13	3.65	1.26	3.57 ± 0.06	3.04	−14.72	0.0319 ± 0.0000	0.0308	−3.39	0.0396 ± 0.0010	0.0435	9.88
5	35	40	72	2.15 ± 0.00	2.37	10.38	2.80 ± 0.03	3.04	8.74	0.0274 ± 0.0003	0.0260	−5.18	0.0460 ± 0.0003	0.0512	11.37
10	45	40	72	4.93 ± 0.20	5.52	11.88	5.17 ± 0.06	4.45	−13.92	0.0191 ± 0.0005	0.0189	−0.80	0.0268 ± 0.0000	0.0310	15.50
10	45	20	24	5.73 ± 0.21	5.02	−12.37	5.50 ± 0.08	4.80	−12.75	0.0200 ± 0.0001	0.0189	−5.26	0.0268 ± 0.0000	0.0289	7.74
15	45	60	72	8.02 ± 0.07	7.39	−7.90	5.02 ± 0.18	5.86	16.64	0.0121 ± 0.0001	0.0111	−8.04	0.0180 ± 2.8 × 10^{-5}	0.0197	9.69
15	45	40	120	6.24 ± 0.05	6.37	2.02	6.64 ± 0.22	6.44	−2.96	0.0120 ± 0.0000	0.0111	−7.28	0.0198 ± 2.4 × 10^{-5}	0.0233	17.71
10	35	20	72	5.53 ± 0.18	5.16	−6.73	5.22 ± 0.00	4.45	−14.75	0.0207 ± 0.0004	0.0181	−12.57	0.0281 ± 2.0 × 10^{-5}	0.0289	2.76
10	45	40	72	5.01 ± 0.02	5.52	10.10	5.16 ± 0.10	4.45	−13.76	0.0208 ± 0.0002	0.0189	−8.90	0.0294 ± 0.0000	0.0310	5.29
10	55	20	72	3.53 ± 0.08	3.83	8.57	4.01 ± 0.03	4.45	10.97	0.0234 ± 0.0000	0.0220	−5.97	0.0270 ± 1.4 × 10^{-5}	0.0289	6.95
5	55	40	72	6.80 ± 0.20	6.96	2.34	3.34 ± 0.64	3.04	−8.84	0.0424 ± 0.0013	0.0379	−10.71	0.0509 ± 7.8 × 10^{-5}	0.0512	0.65
5	45	60	72	5.08 ± 0.07	5.69	11.94	3.28 ± 0.27	3.04	−7.18	0.0326 ± 0.0020	0.0308	−5.47	0.0522 ± 3.7 × 10^{-4}	0.0590	12.94
15	45	20	72	4.64 ± 0.07	5.35	15.20	5.71 ± 0.03	5.86	2.55	0.0126 ± 0.0001	0.0111	−11.69	0.0239 ± 3.3 × 10^{-5}	0.0269	12.42
10	35	60	72	4.84 ± 0.00	3.70	−23.55	4.35 ± 0.06	4.45	2.30	0.0205 ± 0.0000	0.0181	−11.72	0.0295 ± 1.0 × 10^{-5}	0.0330	11.98
10	45	40	72	6.38 ± 0.50	5.52	−13.54	4.11 ± 0.02	4.45	8.27	0.0223 ± 0.0000	0.0189	−15.03	0.0296 ± 1.6 × 10^{-4}	0.0310	4.58
15	55	40	72	6.23 ± 0.27	6.25	0.27	5.12 ± 0.01	5.86	14,.37	0.0121 ± 0.0000	0.0102	−15.73	0.0197 ± 6.7 × 10^{-6}	0.0233	18.30
10	45	60	120	7.27 ± 0.62	7.59	4.38	4.25 ± 0.06	4.10	−3.50	0.0212 ± 0.0003	0.0189	−10.62	0.0295 ± 5.9 × 10^{-5}	0.0330	11.98
15	45	40	24	7.37 ± 0.31	7.94	7.78	6.15 ± 0.15	5.27	−14.35	0.0121 ± 0.0001	0.0111	−8.04	0.0196 ± 4.0 × 10^{-5}	0.0233	18.91
10	55	40	120	8.40 ± 0.15	7.66	−8.87	4.90 ± 0.06	4.10	−16.30	0.0234 ± 0.0000	0.0220	−5.97	0.0265 ± 2.0 × 10^{-5}	0.0310	16.81
10	55	40	24	6.76 ± 0.52	7.13	5.45	4.60 ± 0.03	4.80	4.32	0.0248 ± 0.0001	0.0220	−11.27	0.0264 ± 1.0 × 10^{-5}	0.0310	17.25
10	35	40	24	3.43 ± 0.08	4.95	11.84	4.10 ± 0.06	4.80	17.05	0.0211 ± 0.0009	0.0181	−14.23	0.0266 ± 2.0 × 10^{-5}	0.0310	16.37
10	55	60	72	9.07 ± 0.54	9.37	3.34	4.96 ± 0.11	4.45	−10.28	0.0235 ± 0.0002	0.0220	−6.37	0.0296 ± 1.1 × 10^{-4}	0.0330	11.60
10	45	20	120	6.23 ± 0.03	5.55	−10.95	3.77 ± 0.05	4.10	8.79	0.0170 ± 0.0006	0.0189	11.46	0.0266 ± 2.0 × 10^{-5}	0.0289	8.55
5	45	40	120	6.67 ± 0.95	6.77	1.50	2.13 ± 0.22	1.76	−17.42	0.0354 ± 0.0017	0.0308	−12.95	0.0523 ± 3.6 × 10^{-4}	0.0512	−2.04
				Mathematical Models											
				F	*p*-value		*F*	*p*-value		*F*	*p*-value		*F*	*p*-value	
Intercept				0.804268	0.10792		25.37001	0.000048 *		79.92673	0.000000 *		36.82169	0.000006 *	
A: solid/water (g/100 mL)				11.83276	0.002592 *								18.92259	0.000310 *	
B: temperature (°C)															
C: time (min)				10.10396	0.004720 *					3.90629	0.060776		14.31691	0.001166 *	
D: power (W)							5.31236	0.030989 *					4.26187	0.052190	
A * B				6.53923	0.018784 *					23.36542	0.000079 *				
A * C							2.89507	0.102943					11.05817	0.003374 *	
A * D				4.38972	0.049090 *		4.52823	0.044787 *							
B * C				13.76017	0.001386 *		3.76534	0.065248							
B * D															

Table 2. *Cont.*

Extraction Conditions				Total Phenolic Content (mg Gallic Acid/g gm)						Antioxidant Activity (mmol Trolox/g dm)					
				Chicory By-Product Extracts			Fennel By-Product Extracts			Chicory By-Product Extracts			Fennel By-Product Extracts		
Solid/Water (g/100 mL)	**T (°C)**	**t (min)**	**Power (W)**	**Observed**	**Predicted**	**%var.**	**Observed**	**Predicted**	**%var.**	**Observed**	**Predicted**	**%var.**	**Observed**	**Predicted**	**%var.**
	A^2									6.05110		0.022225 *	22.16692		0.000135 *
	B^2									29.09408		0.000020 *			
	C^2														
	D^2			5.44664		0.030153 *							4.47819		0.057068
Statistics of the Quadratic Models															
Degree of freedom (df)				**6**			**4**			**4**			**6**		
***F*-value**				**6.117842**			**1.558337**			**34.88745**			**40.40381**		
***p*-value**				**0.000909 ***			**0.220484**			**0.000000 ***			**0.000000 ***		
R^2				**0.8473**			**0.9208**			**0.8638**			**0.9238**		

* statistically significant at $p < 0.05$.

Compared to the conventional method, ultrasounds allowed the increase of the TPC of chicory extracts by about 48%, simultaneously reducing the extraction time from 180 to 40 min and the fixed temperature from 60 to 45 °C. This high efficiency can be attributed to the ability of ultrasounds to increase the diffusion of the solvent into the vegetable matrix and to break the cell walls, facilitating the release and the mass transfer [35]. In the case of fennel, the conventional solvent extraction allowed for the recovery of slightly more phenolic compounds than the UAE (+11.7%) by employing a time more than double (90 min vs. 40 min) and working at a higher temperature (65 °C vs. 45 °C). These results are in agreement with the findings of Urango et al. [22].

The antioxidant activity values are reported in Table 2. The AA of chicory extracts were in the range of 0.0120–0.0424 mmol Trolox/g dm, and the extraction conditions that allowed the maximization of this index were the following: solid–water ratio = 5 g/100 mL; T = 55 °C; t = 40 min; power = 72 W. AA of fennel extracts were in the range of 0.0180–0.0534 mmol Trolox/g dm, and the highest values were obtained in the following conditions: solid–water ratio = 5 g/100 mL; T = 45 °C; t = 40 min; power = 24 W.

Compared to the conventional method, ultrasounds allowed the increase in the AA of chicory extracts by about 50%, simultaneously reducing the temperature (from 60 to 55 °C) and prolonging the treatment (from 30 to 40 min). Ultrasounds also allowed the increase (+89%) of AA of fennel extracts, simultaneously reducing the temperature (from 60 to 45 °C) and increasing the time (from 30 to 40 min).

Contrary to what was observed for the conventional extraction, the total phenolic contents of the extracts produced by ultrasounds were not or poorly correlated with their antioxidant activity values, as evidenced by the correlation coefficients (R = 0.2035 for chicory and 0.7173 for fennel). This result can be attributed to the evidence that the various extraction conditions tested (amount and type of thermal energy and the time of treatment) can influence the quantity and type of individual phenolic compounds extracted.

Multiple regression analysis aimed to evaluate the ability of the mathematical model to describe the experimental data and evaluate the influence of the four independent variables on the phenolic content and antioxidant activity of the extracts, identifying the variables that exerted the most significant effects and the extent of these effects. In more depth, the ANOVA of the model and the calculation of R^2, F and p allowed the evaluation of the ability of the model itself to fit the data to a 95% confidence level ($p < 0.05$). The quadratic model excellently described the results observed on chicory extracts ($R^2 = 0.8473$, $p = 0.000909$ for TPC; $R^2 = 0.8638$, $p = 0.000000$ for AA) and the AA values of the fennel extract ($R^2 = 0.9238$, $p = 0.000000$), while the fitting was significant in the case of fennel TPC ($p = 0.220484$) (Table 2). Similarly, through the analysis of variance, the statistical significance of the effects of the independent variables on TPC and AA was measured (Table 2) and the regression coefficients were calculated in order to write the equations describing the relationships between the independent variables and the TPC or AA. The following paragraph describes the results of the analysis of variance separately by matrix.

3.2.1. UAE Extracts of Chicory and Fennel By-Products

Regarding TPC, the following effects were significant ($p < 0.05$): linear effects of 'solid-water ratio' and 'treatment time'; interactive effects of 'solid-water ratio'–'temperature', 'solid-water ratio'–'power', and 'temperature'–'time'; quadratic effects of 'po wer'. Based on the F values, the major impacts on TPC were exerted by 'temperature'–'time' interaction, 'solid-water ratio', and 'time'.

The TPC of chicory extract is described by Equation (4):

$$TPC = +1.5710A - 0.3426C + 0.0003D^2 - 0.0241AB - 0.0044AD + 0.0087BC \quad (4)$$

where A, solid–water ratio (g/100 mL); B, temperature (°C); C, time (min); D, power (W).

According to the equation, the TPC of the extracts increased mainly with the increase in the 'temperature'–'time' interaction, and 'solid-water ratio', while the increase in 'time' determined its reduction. To facilitate the graphic visualization of the effects of the inde-

pendent variables on the TPC, the application of RSM gave rise to six surfaces and related equations that plotted two independent variables at a time, keeping fixed the other two factors at the central value of the experimental design (Figure 1).

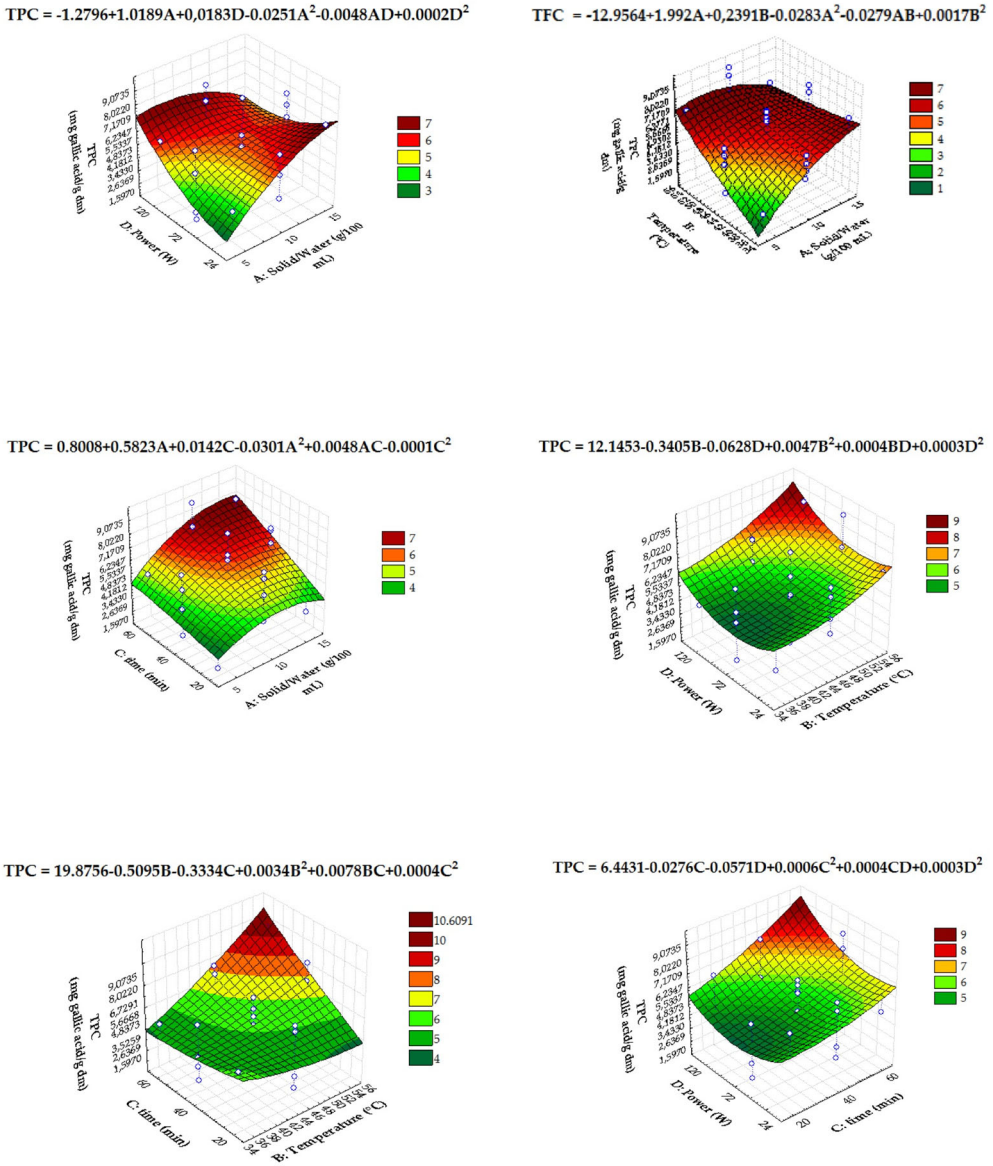


Figure 1. Three-dimensional response surface plots for TPC (mg gallic acid/g dm) of chicory extracts obtained through UAE: effect of solid–water ratio (A), temperature (B), extraction time (C), power (D), and their interactions.

Concerning the antioxidant activity, the following were significant effects ($p < 0.05$): interactive effects of 'solid-water ratio'–'temperature'; quadratic effects of 'solid-water ratio' and 'temperature'. The extraction time did not exert significant effects. According to the F values, the major impacts on AA were exerted by both the quadratic 'temperature' term and the interactive 'solid-water ratio'–'temperature' term.

The AA of chicory extract is described by Equation (5):

$$AA = 0.0244 + 0.00009A^2 + 0.00001B^2 - 0.00008AB \quad (5)$$

where A, solid–water ratio (g/100 mL); B, temperature (°C).

Based on the equation, the antioxidant activity mainly increased with 'temperature' and decreased as the 'solid-water ratio'–'temperature' interaction increased. The corresponding six-response surfaces and equations are reported in Figure S1.

Concerning fennel, statistically significant effects ($p < 0.05$) on TPC were exerted by the linear term 'power' and the interactive term of 'solid-water ratio'–'power'. Based on the *F* values, their impacts were similar. The interactions 'solid-water ratio'–'time' and 'temperature'–'time' were not statistically significant.

The TPC of fennel extract is described by Equation (6), while the response surfaces are shown in Figure S2.

$$TPC = 4.9733 - 0.0463D + 0.0039AD \quad (6)$$

where A, solid–water ratio (g/100 mL); D, power (W).

According to Equation (6), the total phenolic content of fennel extracts decreased with the increasing values of 'power', and increased with the increase in the 'solid-water ratio'–'power' interactive term.

Concerning the antioxidant activity of fennel extracts, significant effects ($p < 0.05$) were exerted by the linear and quadratic 'solid-water ratio' term, the linear 'time' term and the interactive 'solid-water ratio'–'time' term. The linear and quadratic 'power' terms were not statistically significant. According to the *F* values, the major impacts on AA were exerted by the quadratic 'solid/water' term, followed by the linear 'solid-water ratio' and 'time' terms and their interaction.

The AA of fennel extract is described by Equation (7), which shows that the antioxidant activity increased with the increase in the quadratic 'solid-water ratio' and the linear 'time' terms, and decreased with the increase in the linear 'solid-water ratio' term and in the interaction between 'solid-water ratio' and 'time'. The response surfaces obtained with the application of RSM are shown in Figure S3.

$$AA = 0.0574 - 0.0056A + 0.0007C + 0.0002A^2 - 0.00006AC \quad (7)$$

where A, solid–water ratio (g/100 mL); C, time (min).

3.2.2. Predictive Ability of the Models Applied to UAE

In addition to the observed results, Table 2 also reports the values predicted by the models for TPC and AA, respectively. In general, the predicted values were in good agreement with the experimental results since all conditions tested in all models showed a variation between observed and predicted values lower than 20%. The correlation coefficients R between observed and predicted values were the following: 0.9380 and 0.8760 for the TPC of chicory and fennel, respectively; 0.9866 and 0.9841 for the AA of chicory and fennel, respectively. According to these data, the models proposed appeared satisfactory and accurate.

3.3. Results of Microwave-Assisted Extraction

The TPC values obtained by applying the three-factor, three-levels BBD are reported in Table 3. The total phenolic contents of chicory extracted by microwaves were in the range of 3.66–8.23 mg gallic acid/g dm, and the extraction conditions that allowed the maximization of this index were the following: solid–water ratio = 7.5 g/100 mL; t = 2 min; power = 350 W. This result is better than those (6.35 ± 0.10 mg/g dm) obtained by Jangra and Madan [36] applying the following conditions: solid-methanol ratio = 5 g/100 mL; t = 10 s; power = 320 W. The total phenolic contents of fennel extracts were in the range of 3.89–6.73 mg gallic acid/g dm, and the highest values were obtained in the following conditions: solid–water ratio = 7.5 g/100 mL; t = 3 min; power = 160 W. Once again, the experimental results were better than those extracted from the literature. As an example, Di Donato et al. [37] recovered 4.11 ± 0.36 mg/g dm by applying a MAE using a household microwave oven under the following conditions: solid–alcohol ratio = 4 g/100 mL; t = 5 min; power = 750 W.

Table 3. Development of the Box–Behnken experimental design for microwave-assisted extraction: experimental results (observed) and values predicted by the models for total phenolic content and antioxidant activity; analyses of variance for linear, quadratic, and interactive effects of the independent variables and the determination coefficients of the models.

Extraction Conditions			Total Phenolic Content (mg Gallic Acid/g gm)						Antioxidant Activity (mmol Trolox/g dm)					
			Chicory By-Product Extracts			Fennel By-Product Extracts			Chicory By-Product Extracts			Fennel By-Product Extracts		
Solid/Water (g/100 mL)	**t (min)**	**Power (W)**	**Observed**	**Predicted**	**%var.**	**Observed**	**Predicted**	**%var.**	**Observed**	**Predicted**	**%var.**	**Observed**	**Predicted**	**%var.**
7.5	2	350	7.74 ± 0.28	8.7415	12.94	5.74 ± 0.35	6.08	5.94	0.0224 ± 0.0002	0.0237	5.63	0.0352 ± 0.0000	0.0358	1.75
5	2	160	5.70 ± 0.59	5.8946	3.41	5.02 ± 0.36	5.09	1.49	0.0313 ± 0.0014	0.0279	−10.99	0.0528 ± 0.000	0.0494	−6.42
5	3	350	7.44 ± 0.28	8.8431	18.86	5.48 ± 0.28	5.09	−7.03	0.0329 ± 0.0006	0.0279	−15.32	0.0426 ± 0.0010	0.0494	15.99
7.5	2	350	8.23 ± 0.20	8.7415	6.21	5.88 ± 0.14	6.08	3.42	0.0249 ± 0.0007	0.0237	−4.98	0.0349 ± 0.0000	0.0358	2.62
7.5	3	160	5.15 ± 0.24	5.7929	12.48	6.73 ± 0.30	6.08	−9.65	0.0247 ± 0.0004	0.0237	−4.21	0.0353 ± 0.0000	0.0358	1.46
2.5	1	160	4.11 ± 0.27	4.7912	16.58	4.95 ± 1.38	4.11	−17.00	0.0329 ± 0.0001	0.0321	−2.55	0.0531 ± 0.0020	0.0576	8.42
5	2	160	5.57 ± 0.10	5.8946	5.83	6.16 ± 0.24	5.09	−17.30	0.0293 ± 0.0013	0.0279	−4.91	0.0531 ± 0.0000	0.0494	−6.95
2.5	2	90	3.66 ± 0.33	3.7049	1.23	4.47 ± 0.76	4.11	−8.09	0.0286 ± 0.0019	0.0321	12.10	0.0671 ± 0.0000	0.0576	−14.20
5	1	90	5.02 ± 0.07	4.8083	−4.22	4.95 ± 0.09	5.09	2.92	0.0286 ± 0.0007	0.0279	−2.59	0.0528 ± 0.0000	0.0494	−6.42
2.5	2	90	3.84 ± 0.40	3.7049	−3.52	3.96 ± 0.19	4.11	3.75	0.0375 ± 0.0022	0.0321	−14.51	0.0498 ± 0.0010	0.0576	15.60
2.5	1	160	4.06 ± 0.21	4.7912	18.01	3.89 ± 0.14	4.11	5.61	0.0338 ± 0.0003	0.0321	−5.15	0.0578 ± 0.0050	0.0576	−0.40
5	3	350	7.91 ± 0.21	8.8431	11.80	6.33 ± 0.25	5.09	−19.52	0.0265 ± 0.0054	0.0279	5.13	0.0527 ± 0.0000	0.0494	−6.24
7.5	3	160	5.45 ± 0.02	5.7929	6.29	6.01 ± 0.08	6.08	1.18	0.0242 ± 0.0017	0.0237	−2.23	0.0352 ± 0.0000	0.0358	1.75
5	1	90	4.74 ± 0.26	4.8083	1.44	4.49 ± 0.30	5.09	13.47	0.0255 ± 0.0020	0.0279	9.25	0.0459 ± 0.0020	0.0494	7.65
5	2	160	5.26 ± 0.20	5.8946	12.06	5.68 ± 0.30	5.09	−10.31	0.0288 ± 0.0014	0.0279	−3.26	0.0530 ± 0.0000	0.0494	−6.77
			Mathematical Models											
			F	*p*-value		*F*	*p*-value		*F*	*p*-value		*F*	*p*-value	
Intercept			0.94309	0.359927		11.37521	0.004998 *		130.7809	0.000000 *		648.6510	0.000000 *	
A: solid/water (g/100 mL)			15.06193	0.004668 *		5.14653	0.040975 *		7.9544	0.014455 *				
B: time (min)			2.69053	0.139576										
C: power (W)			4.89658	0.047826 *										
A * B														
A * C														
B * C														
A^2			10.77116	0.011155 *								38.7114	0.000031 *	
B^2			2.13493	0.182111										
C^2			2.74431	0.136192										
			Statistics of the Quadratic Models											
Degree of freedom (df)			**6**			**1**			**1**			**1**		
***F*-value**			**14.25905**			**5.146529**			**7.954352**			**38.71144**		
***p*-value**			**0.000696 ***			**0.040975 ***			**0.014455 ***			**0.000031**		
R^2			**0.9145**			**0.7836**			**0.9796**			**0.7486**		

* statistically significant at $p < 0.05$.

Compared to the conventional method, the MAE allowed the increase of the TPC of chicory extracts by about 34%, simultaneously reducing the extraction time from 180 to 2 min and reaching, at the end of treatment, a temperature of 50 °C (vs. 60 °C of the conventional treatment). In the case of fennel, the conventional solvent extraction allowed the recovery of slightly more phenolic compounds than the MAE (+10.5%), simultaneously reducing the extraction time from 180 to 3 min and reaching, at the end of treatment, a temperature of 40 °C (vs. the 60 °C of the conventional treatment). This high efficiency can be attributed to the ability of microwaves to heat the inner part of the plant matrix to increase the pressure inside the cells, thus resulting in cell wall disruption and in the release of bioactive compounds [38]. A study by Akhtar et al. [39] has already highlighted the highest extraction efficiency of MAE with respect to the Soxhlet extraction and cold maceration regarding the phenolic fraction of fennel seeds, suggesting that microwaves do not degrade these compounds due to lesser treatment time.

The antioxidant activity values of MAE extracts are also reported in Table 3. The AA of chicory extracts were in the range of 0.0224–0.0375 mmol Trolox/g dm and the extraction conditions that allowed the maximization of this index were the following: solid–water ratio = 2.5 g/100 mL; t = 2 min; power = 90 W. The AA of fennel extracts were in the range of 0.0349–0.0671 mmol Trolox/g dm, and the highest values were obtained in the same conditions as those of the chicory extracts.

Compared to the conventional method, ultrasounds allowed the increase of the AA of chicory extracts by about 33%, simultaneously reducing the time of treatment (from 30 to 2 min). Microwaves also determined a strong increase (+138%) of the AA of fennel extracts, simultaneously reducing the time of treatment (from 30 to 2 min).

Similar to what was observed for the UAE, the total phenolic contents of the extracts produced by microwaves were poorly correlated with the antioxidant activity values, as highlighted by the correlation coefficients (R = 0.4906 and 0.5601 for chicory and fennel, respectively).

According to the ANOVA results at $p < 0.05$ (Table 3), the quadratic model excellently described the experimental data of both chicory ($R^2 = 0.9145$ and $R^2 = 0.9796$ for TPC and AA, respectively) and fennel extracts obtained through MAE ($R^2 = 0.7836$ for total phenolics and $R^2 = 0.7486$ for the antioxidant activity). The discussion concerning the statistical significance of the effects of the independent variables and the regression coefficients (Table 3) are reported in the following paragraph.

3.3.1. MAE Extracts of Chicory and Fennel By-Products

Regarding the TPC, the following effects were significant ($p < 0.05$): linear and quadratic effects of 'solid-water ratio' and linear effect of 'power'. The linear and quadratic effects of 'time' and quadratic effects of 'power' were not significant. Based on the *F* values, the major impacts on TPC were exerted by linear and quadratic 'solid-water ratio' terms.

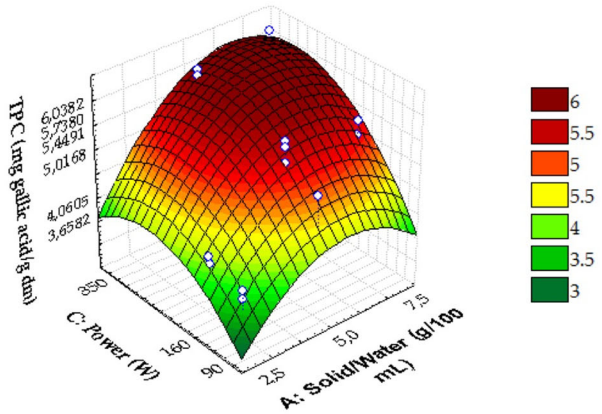
The TPC of chicory extracted by MAE is described by Equation (8):

$$TPC = 1.1643A + 0.0155C - 0.0964A^2 \quad (8)$$

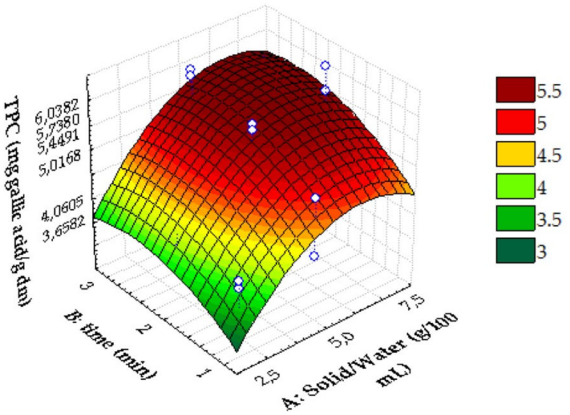
where A, solid–water ratio (g/100 mL); C, power (W).

According to the equation, the TPC of the extracts increased mainly with the increase in the linear 'solid-water ratio' and 'power' terms, and decreased with the increase in the quadratic 'solid-water ratio' term. To allow the graphic visualization of the effects of the independent variables on the TPC, the application of RSM gave rise to three surfaces and the related equations that plotted two independent variables at a time, keeping fixed the other factor at the central value of the experimental design (Figure 2).

$$TPC = -0.135+1.2291A+0.0158C-0.1146A^2+0.0008AC-3.3542E-5C^2$$



$$TPC = -0.109+1.2465A+1.4357B-0.103A^2+0.033AB-0.3095B^2$$



$$TPC = 1.2505+1.5278B+0.0174C-0.4431B+0.0032BC-4.1239E-5C^2$$

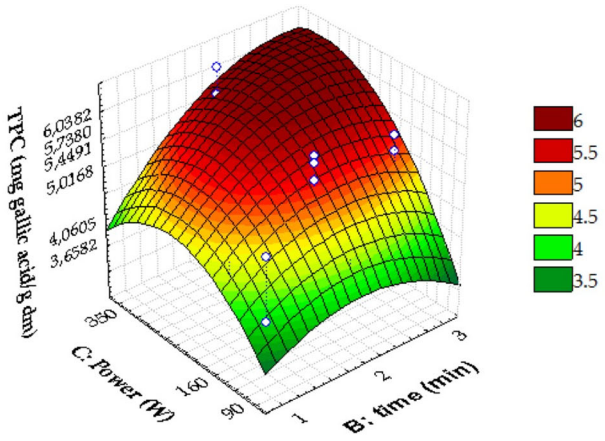


Figure 2. Three-dimensional response surface plots for TPC (mg gallic acid/g dm) of chicory extracts obtained through MAE: effect of solid–water ratio (A), extraction time (B), power (C), and their interactions.

Concerning the antioxidant activity, only the linear 'solid-water ratio' term was significant ($p < 0.05$), and the equation that describes the results is the following (9):

$$AA = 0.0363 - 0.0017A \quad (9)$$

where A, solid–water ratio (g/100 mL).

As can be inferred from the regression coefficients, the antioxidant activity decreased as the 'solid-water ratio' increased. The response surfaces are shown in Figure S4.

Concerning the fennel, the linear 'solid-water ratio' term was the only one to exert a statistically significant effect on fennel TPC. The total phenolic content of fennel extracted by MAE is described by Equation (10), which highlights that its increase was associated with the increase in the 'solid-water ratio'. Figure S5 shows the visual representation of the response surfaces.

$$TPC = 3.1220 + 0.3945A \quad (10)$$

where A, solid–water ratio (g/100 mL).

The antioxidant activity of the fennel extracts was significantly affected only by the quadratic 'solid-water ratio' term and, according to Equation (11), the AA decreased with the increase in the 'solid-water ratio'. The response surfaces that visually describe the relationships between dependent and independent variables are shown in Figure S6.

$$AA = 0.0603 - 0.0004A^2 \quad (11)$$

where A, solid–water ratio (g/100 mL).

3.3.2. Predictive ability of the models applied to MAE

The values predicted by the models for TPC and AA are reported in Table 3. The predicted values are in agreement with the experimental results since the variation between the observed and predicted values was lower than 20%. The correlation coefficients R between the observed and predicted values were the following: 0.9808 and 0.8155 for TPC and AA of chicory extracts; 0.7734 and 0.8811 for TPC and AA of fennel extracts. According to these data, the models were able to satisfactorily describe the experimental data concerning chicory by-products.

3.3.3. Final Consideration on the Influence of the Independent Variables on the Phenolic Content and Antioxidant Activity of the Extracts

At the end of the presentation of the results, it emerges that the solute-to-water ratio was the parameter that most influenced the TPC and AA of the extracts, sometimes positively (TPC and AA of chicory submitted to UAE; TPC of fennel submitted to MAE), sometimes decreasing them (TPC of chicory submitted to MAE; AA of chicory and fennel submitted to MAE). This behaviour is due to the fact that the volume of the solvent must be sufficient to permit good hydration and swelling of the matrix without running into excessive dilution that also would affect the cost-efficiency of the operation [21]. Concerning UAE extraction, temperature, time and their interactions contributed to the increase in TPC and AA by increasing solubility and mass transfer, in agreement with the findings of Boonkird et al. [40] and Galvan d'Alessandro et al. [41].

3.4. Phenolic Profiles of the Extracts

The examples of the sample phenolic profiles are reported in Figure 3. Table 4 reports the phenolic profiles of the extracts obtained for each technique under the conditions that allowed to maximize the relative TPCs. LOD and LOQ were calculated for each phenolic compound, with the first ranging from 0.11 to 0.32 mg/L and the latter ranging between 0.45 and 0.95 mg/L.

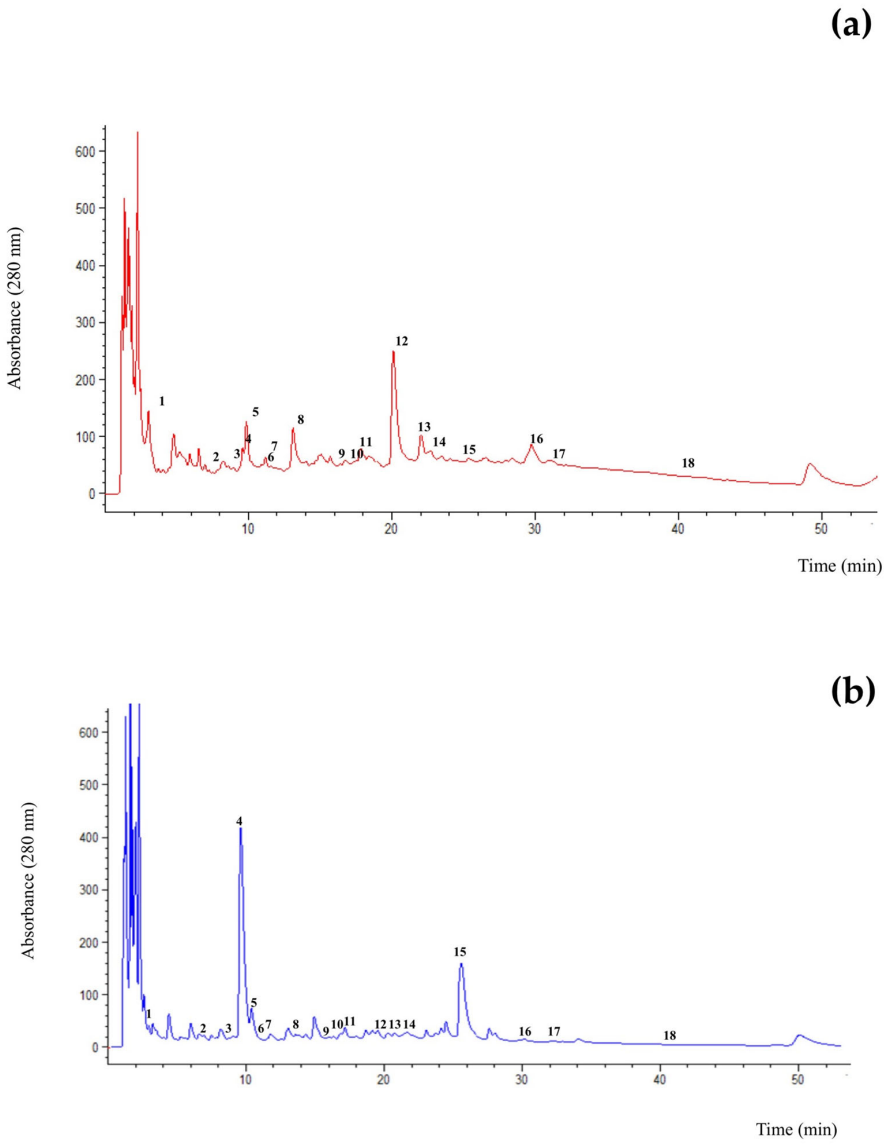


Figure 3. Phenolic profiles acquired at 280 nm, of (**a**) chicory and (**b**) fennel extracts obtained by applying UAE under the conditions that allowed the maximization of the relative TPCs. 1: Gallic acid; 2: 4-Hydroxybenzoic acid; 3: Catechin; 4: Vanillic acid; 5: Caffeic acid; 6: Syringic acid; 7: Epicatechin; 8: Chlorogenic acid; 9: Epigallocatechin; 10: Ferulic acid; 11: *p*-Coumaric acid; 12: Sinapic acid; 13: Epicatechingallate; 14: Rutin; 15: Resveratrol; 16: Rosmarinic acid; 17: Quercetin; 18: Kaempferol.

Regarding chicory by-products: 14 peaks were identified in conventional extracts, with epigallocatechin, rutin, sinapic acid and epicatechin occurring in higher concentrations; 17 compounds were identified in UAE extracts, with rosmarinic, sinapic, and chlorogenic acid as the most representative phenolics; the MAE extracts showed the simpler profile with only eight peaks, and epicatechin and rosmarinic acid as the main phenolics. With respect to the other extraction system, the conventional system allowed the extraction of more 4-hydroxybenzoic, *p*-coumaric and vanillic acids, as well as rutin, catechin, and epigallocatechin. UAE was more effective in the extraction of gallic, rosmarinic, sinapic and chlorogenic acids, as well as quercetin and epigallocatechingallate. No compound was extracted to a greater extent through the application of MAE.

Table 4. The phenolic profiles of the extracts corresponding to the combinations of independent variables able to maximize the total phenolic concentrations. Data are expressed as mg/g dm.

Phenolic Compounds (Retention Time in min)	Extraction Techniques					
	Conventional		UAE		MAE	
	Chicory T: 60 °C t: 180 min	Fennel T: 60 °C t: 90 min	Chicory Solid/Water: 10 g/100 mL T: 55 °C t: 60 min Power: 72 W	Fennel Solid/Water: 5 g/100 mL T: 45 °C t: 40 min Power: 24 W	Chicory Solid/Water: 7.5 g/100 mL t: 2 min Power: 350 W	Fennel Solid/Water: 7.5 g/100 mL t: 3 min Power: 160 W
Gallic acid (3.04)	n.d. ^{a}	n.d. ^{A}	0.052 ± 0.010 ^{b}	0.022 ^{A} ± 0.001	0.011 ± 0.000 ^{a}	0.010 ± 0.000 ^{A}
4-Hydoxybenzoic acid (7.20)	0.058 ± 0.001 ^{b}	n.d. ^{A}	0.022 ± 0.001 ^{a}	0.023 ± 0.001 ^{A}	0.010 ± 0.001 ^{a}	n.d. ^{A}
Catechin (8.24)	0.204 ± 0.003 ^{b}	0.019 ± 0.001 ^{AB}	0.049 ± 0.014 ^{a}	n.d. ^{A}	0.030 ± 0.003 ^{a}	0.040 ± 0.002 ^{B}
Vanillic acid (9.36)	0.060 ± 0.001 ^{b}	0.085 ± 0.001 ^{B}	0.022 ± 0.002 ^{a}	0.011 ± 0.001 ^{A}	0.010 ± 0.002 ^{a}	n.d. ^{A}
Caffeic acid (10.14)	0.017 ± 0.001 ^{a}	0.009 ± 0.001 ^{A}	0.031 ± 0.001 ^{a}	0.039 ± 0.001 ^{B}	0.020 ± 0.001 ^{a}	0.053 ± 0.003 ^{B}
Syringic acid (11.13)	0.018 ± 0.001 ^{a}	n.d. ^{A}	n.d. ^{a}	n.d. ^{A}	n.d. ^{a}	0.012 ± 0.001 ^{A}
Epicatechin (11.97)	0.181 ± 0.069 ^{b}	0.077 ± 0.001 ^{A}	0.174 ± 0.033 ^{b}	0.139 ± 0.008 ^{B}	0.100 ± 0.000 ^{a}	3.729 ± 0.072 ^{C}
Chlorogenic acid (12.35)	n.d. ^{a}	n.d. ^{A}	0.321 ± 0.014 ^{b}	n.d. ^{A}	n.d. ^{a}	0.022 ± 0.000 ^{A}
Epigallocatechin (16.00)	0.537 ± 0.001 ^{b}	n.d. ^{A}	0.012 ± 0.000 ^{a}	n.d. ^{A}	n.d. ^{a}	0.100 ± 0.002 ^{B}
Ferulic acid (16.31)	0.038 ± 0.001 ^{a}	n.d. ^{A}	0.029 ± 0.002 ^{a}	0.038 ± 0.000 ^{B}	0.040 ± 0.001 ^{a}	0.030 ± 0.000 ^{B}
p-Coumaric acid (16.83)	0.093 ± 0.005 ^{c}	n.d. ^{A}	0.043 ± 0.001 ^{b}	0.018 ± 0.001 ^{A}	n.d. ^{a}	0.011 ± 0.000 ^{A}
Sinapic acid (20.68)	0.258 ± 0.007 ^{b}	0.161 ± 0.001 ^{B}	0.789 ± 0.035 ^{c}	0.029 ± 0.001 ^{A}	n.d. ^{a}	0.010 ± 0.000 ^{A}
Epigallocatechingallate (21.57)	n.d. ^{a}	0.148 ± 0.001 ^{B}	0.155 ± 0.003 ^{b}	n.d. ^{A}	n.d. ^{a}	n.d. ^{A}
Rutin (22.14)	0.355 ± 0.001 ^{c}	0.040 ± 0.001 ^{A}	0.143 ± 0.031 ^{b}	0.025 ± 0.004 ^{A}	n.d. ^{a}	0.030 ± 0.002 ^{A}
Resveratrol (25.90)	0.032 ± 0.001 ^{b}	0.046 ± 0.001 ^{A}	0.029 ± 0.004 ^{b}	0.047 ± 0.002 ^{A}	n.d. ^{a}	0.040 ± 0.001 ^{A}
Rosmarinic acid (29.50)	n.d. ^{a}	n.d. ^{A}	1.527 ± 0.088 ^{b}	n.d. ^{A}	0.071 ± 0.011 ^{a}	n.d. ^{A}
Quercetin (31.70)	0.04 ± 0.002 ^{b}	0.021 ± 0.000 ^{A}	0.082 ± 0.002 ^{c}	0.029 ± 0.000 ^{A}	n.d. ^{a}	0.019 ± 0.001 ^{A}
Kaempferol (40.07)	0.017 ± 0.001 ^{a}	n.d. ^{A}	0.013 ± 0.001 ^{a}	n.d. ^{A}	n.d. ^{a}	0.060 ± 0.002 ^{B}

In rows, different superscript lowercase letters correspond to statistically significant differences between the extraction techniques applied to chicory by-products, while different superscript uppercase letters correspond to statistically significant differences between the extraction techniques applied to fennel by-products ($p < 0.05$); n.d.: not detected.

Concerning fennel by-products, nine compounds were identified in conventional extracts, with sinapic acid and epigallocatechingallate present in higher concentrations; 11 peaks were identified in extracts obtained through ultrasounds, with epicatechin being the most representative phenolic compound; 14 compounds were recognized in MAE extracts, with epicatechin present in the highest concentrations. Compared to the other extraction techniques, the conventional system allowed a greater extraction of vanillic and sinapic acids, as well as epigallocatechingallate, while MAE was more able to extract catechin, epicatechin, epigallocatechin and kaempferol. Ferulic and caffeic acids were better extracted by both UAE and MAE.

Independent of the extraction method, the aqueous extracts of chicory and fennel by-products are confirmed as an easily available source of dietary polyphenols [42].

As can be inferred from these data, the highest number of compounds was recognized in UAE, followed by conventional extracts and MAE extracts. In more depth, the extraction techniques influenced not only the extraction yield but also the number, type and concentrations of the individual phenolic compounds, and the effects depended on the matrices. These results are in agreement with those of Rocchetti et al., who highlighted that each extraction technique among those that they decided to apply to *Moringa oleifera* leaves (maceration, homogenizer-assisted extraction, solid/liquid dynamic extraction, microwave-assisted extraction and ultrasound-assisted extraction) promoted the recovery of specific phenolic subclasses with different efficiencies [43]. These findings are also related to the separation properties of phenolic compounds, which are in turn affected by their structural characteristics. It is known that the structures of polyphenols influence their polarity, conjugation and interaction with the sample matrix, and in turn their propensity to be extracted with a particular extraction procedure since each extraction technique is based on peculiar operating principles. According to a review of Alara et al. [44], UAE treatments rely on the ability of micro-sized bubble explosions to give a quick disorganization of tissues, thus facilitating the diffusion of polyphenols (mainly rosmarinic and carnosic acids, as well as anthocyanins) from substance into the solvent. Instead, with the application of MAE, the heat generated by microwaves, increases solvent diffusion and helps the rupture of hydrogen bonds, thus being effective in the extraction of short-chain polyphenols, such as phenolic acid sand flavonoids, and detrimental in the extraction of polymeric compounds due to the possibility of destroying molecules, having many hydroxyl-type substituents in their structure and heat-sensitive phenolics (anthocyanins, for example), especially when the temperature increases due to the application of high-power values for long periods of time.

4. Conclusions

The application of the Box–Behnken design and response surface methodology to the ultrasound- and microwave-assisted extraction of antioxidant compounds from chicory and fennel by-products were effective tools to study the impacts of the process variables and to optimize the extraction conditions. The efficiency of the sustainable techniques depended on the matrix. Compared to a conventional extraction performed with a 70% ethanol aqueous solution as extraction solvent, UAE and MAE performed with water as solvent allowed the obtainment of chicory extracts richer in phenolic compounds (+48% and +34%, respectively), significantly decreasing the extraction times (4-fold and 90-fold reduction, respectively.) Regarding the fennel, the application of UAE and MAE determined the extraction of a slightly lower amount of phenolics (−11.7% and −10.5%, respectively) but halving the extraction time (UAE) or reducing it 60-fold (MAE). Based on these findings, microwave-assisted extraction seems to be the most sustainable technique. The solid–water ratio was the variable with the highest effect in models applied to microwave-assisted extraction and it was one of the main variables affecting ultrasound-assisted extraction, contributing sometimes positively and sometimes negatively to the extraction of antioxidant compounds. The applications of the models allowed the prediction of TPC and AA values close to the experimental results, thus proving the adequacy of models

themselves. Extraction techniques strongly affected the number, amount and type of phenolic compounds extracted, and were beyond consideration relating to sustainability aspects; this information can guide the choice of extraction technique based on the type of phenolic profile that is to be obtained.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app13074191/s1, Figure S1: 3D response surface plots for antioxidant activity (mmol Trolox/g dm) of chicory extracts obtained through UAE: effect of solid–water ratio (A), temperature (B), extraction time (C), power (D), and their interactions; Figure S2: 3D response surface plots for TPC (mg gallic acid/g dm) of fennel extracts obtained through UAE: effect of solid–water ratio (A), temperature (B), extraction time (C), power (D), and their interactions; Figure S3: 3D response surface plots for antioxidant activity (mmol Trolox/g dm) of fennel extracts obtained through UAE: effect of solid–water ratio (A), temperature (B), extraction time (C), power (D), and their interactions; Figure S4: 3D response surface plots for antioxidant activity (mmol Trolox/g dm) of chicory extracts obtained through MAE: effect of solid–water ratio (A), extraction time (B), power (C), and their interactions; Figure S5: 3D response surface plots for TPC (mg gallic acid/g dm) of fennel extracts obtained through MAE: effect of solid–water ratio (A), extraction time (B), power (C), and their interactions; Figure S6: 3D response surface plots for antioxidant activity (mmol Trolox/g dm) of fennel extracts obtained through MAE: effect of solid–water ratio (A), extraction time (B), power (C), and their interactions.

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Abbreviation

AA	Antioxidant activity
ANOVA	Analysis of variance
BBD	Box–Behnken design
DPPH	2,2-diphenyl-1-picrylhydrazyl
FC	Folin–Ciocalteu
LSD	Least significant difference
MAE	Microwave-assisted extraction
RSM	Response surface methodology
TPC	Total phenolic content
Trolox	6-hydroxy-2,5,7,8-tetramethylchroman2-carboxylic acid
UAE	Ultrasound-assisted extraction

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