

Article

Crack the Shell by Unlocking the Polyphenol Power of Hazelnut Waste with Ultrasound

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Abstract

Hazelnut (*Corylus avellana* L.) shells, typically discarded as agro-industrial by-products, represent a potentially valuable source of bioactive polyphenolic compounds with significant antioxidant properties. This study aimed to evaluate and compare the polyphenol composition and antioxidant capacity of the kernels and shells of two hazelnut varieties, ‘Rimski’ and ‘Istarski duguljasti’. High-intensity ultrasound-assisted extraction (UAE) was applied to enhance the recovery of bioactive compounds under optimized conditions (80% ethanol, high amplitude, and 25 min treatment). The extracts were analyzed for total polyphenols, total flavonoids, total non-flavonoids, and individual phenolic compounds. Hazelnut shells exhibited significantly higher levels of total polyphenols, flavonoids, and antioxidant capacity compared to kernels. The dominant individual polyphenolic compounds identified in the shell were kaempferol, gallic acid, naringin, rutin trihydrate, quercetin-3-glucoside, chlorogenic acid, quercetin, ferulic acid, rosmarinic acid, and vanillic acid. Application of UAE notably improved extraction efficiency and overall yield compared to conventional extraction methods. The findings underscore hazelnut shells as a nutritionally and functionally valuable by-product and confirm UAE as a green, efficient extraction technique. These results provide a strong basis for developing high-value-added products for the cosmetic, pharmaceutical, and food industries, thereby supporting circular bioeconomy and sustainable chemistry principles.

Keywords: hazelnut shell; polyphenols; high-intensity ultrasound; antioxidant capacity; green extraction; circular bioeconomy



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1. Introduction

Over the past few decades, there has been a strong shift from linear production models (“take–make–dispose”) towards circular and sustainable approaches within the agri-food sector [1,2]. Special emphasis is placed on the valorization of agricultural by-products as renewable resources that can contribute to a more sustainable bio-based economy. One such by-product is the hazelnut shell (*Corylus avellana* L.), which is generated in large amounts during the industrial processing of hazelnuts and is typically discarded, used as low-value biomass, or simply burned for energy [3]. This practice results in the loss of potentially valuable bioactive compounds and materials that could be used to produce high-value products. The hazelnut shell represents a significant proportion of the total

fruit mass, approximately 43% to 55% according to different studies [4–6], indicating that for every tonne of hazelnuts processed, several hundred kilograms of shell are produced as waste. Global hazelnut production has exceeded 1.1 million tonnes (in-shell) annually, which translates into hundreds of thousands of tonnes of shells generated each year [6]. Consequently, finding sustainable strategies for their recovery and valorization has become an important environmental and economic challenge.

Hazelnut shells are chemically classified as lignocellulosic materials, with cellulose, hemicellulose, and lignin as the predominant structural components. In addition, they contain various bioactive phenolic compounds, such as phenolic acids and flavonoids [6–8]. Recent studies have identified up to 18 different phenolic constituents in hazelnut shell extracts, with gallic acid being among the most abundant. Moreover, strong correlations between total phenolic content (TPC) and antioxidant capacity have been observed, suggesting that this underutilized matrix has considerable potential for producing natural antioxidants and functional ingredients [3,9,10]. These bioactive compounds could be recovered and applied in the formulation of nutraceuticals, bio-based adsorbents, active food packaging materials, and other high-value bioproducts, aligning with the principles of circular bioeconomy. In this context, the use of environmentally friendly or “green” extraction techniques are of particular importance. Ultrasonic-assisted extraction (UAE) has emerged as an efficient and sustainable method for isolating phenolic compounds from plant matrices, allowing higher extraction yields at lower temperatures and shorter processing times compared to conventional techniques [11–13]. The effectiveness of UAE is mainly attributed to acoustic cavitation, which generates localized high-pressure and high-temperature microenvironments, leading to cell wall disruption, enhanced solvent penetration, and improved mass transfer. Cavitation intensity and energy density are influenced by ultrasound amplitude, frequency, and extraction time, which together determine the extent of matrix disintegration and release of bound phenolic compounds. These effects are particularly relevant for lignocellulosic materials such as hazelnut shells, where phenolics are often associated with structural polymers [11,13–15]. Moreover, ethanol–water mixtures are considered safe, renewable, and cost-effective solvent systems that align with green chemistry principles. Recent advances in sustainable extraction also highlight the potential of natural deep eutectic solvents (NADESs) and other deep eutectic solvent (DES) systems, which are biocompatible, biodegradable, and enable selective extraction of phenolic compounds with minimal environmental impact [7,16]. Supercritical CO₂ extraction offers another environmentally friendly alternative, allowing solvent-free recovery of lipophilic antioxidants under mild temperature conditions. Microwave-assisted extraction (MAE) and enzyme-assisted extraction (EAE) represent additional green approaches, reducing processing time and solvent consumption while maintaining high extraction efficiency. Furthermore, combinations of these techniques (e.g., UAE–NADES or MAE–DES) have been shown to synergistically enhance polyphenol recovery, demonstrating the growing potential of integrated green extraction strategies for valorizing plant by-products. The adoption of such methods not only improves the yield and quality of bioactive compounds but also aligns with the principles of sustainable chemistry, minimizing environmental impact and promoting resource efficiency [17–19].

In the present study, two hazelnut cultivars were analyzed to assess the valorization potential of their kernels and shells. Powdered shells of each were subjected to ultrasonic-assisted extraction, in which solvent composition (50% and 80% ethanol, *v/v*), amplitude (40 and 60%), and extraction time (10, 15 and 25 min) were varied. The obtained extracts were then analyzed for total phenolic content (TPC), total flavonoid content (TFC), total non-flavonoid content (TNFC), individual phenolic compounds by high-performance liquid chromatography (HPLC), and antioxidant capacity. This study aims to provide

a deeper understanding of the bioactive potential of hazelnut shells as a promising raw material for the production of high-value natural extracts. By applying a green extraction approach and comparing different process parameters, the work contributes to the development of sustainable methods enabling the valorization of agricultural by-products into value-added bio-based materials in line with waste reduction strategies and circular bioeconomy principles.

2. Materials and Methods

2.1. Plant Material

For this research, two varieties of hazelnut (*Corylus avellana* L.), ‘Rimski’ and ‘Istarski duguljasti’ [20], from a 17-year-old plantation located on a family farm near Sisak, Croatia, were used. In the hazelnut plantation, standard agrotechnical practices were regularly applied, including mechanical weed control, manual pruning of shoots, and the maintenance of a tree-like growth form. Hazelnuts were collected in October during the 2024 vegetation season. After harvesting, the shells were separated from the kernels using a specialized machine, and samples were immediately delivered to the Laboratory for Quality Analysis of Agricultural Products of Plant Origin at the Department of Sustainable Technologies and Renewable Energy Sources, University of Zagreb Faculty of Agriculture. After separation, each component (shell and kernel) for both hazelnut varieties was weighed individually, and the percentage of kernel and shell was calculated. The samples were then processed immediately without any drying step, ground, and used for further analyses. For further extraction processes, the shells of each variety were ground separately using a mill (self-built, manually operated) and a laboratory homogenizer (IKA UltraTurrax T-18, Staufen, Germany) and sieved through a self-built sieve to obtain a powder of visually uniform consistency with particles smaller than 1 mm.

2.2. Classical and Ultrasound-Assisted Extraction of Hazelnut Shell

Different procedures were used to evaluate the influence of extraction type and conditions on the yield of phenolic compounds and the antioxidant capacity of hazelnut shells. Two extraction methods were applied: conventional and ultrasound-assisted extraction (UAE). Milled hazelnut shells were used to prepare extracts by both methods. For each extraction, $4 \text{ g} \pm 0.01$ of milled shell material was weighed into 150 mL beakers, and 100 mL of solvent was added. Two ethanol concentrations were used as extraction solvents: 50 and 80% (*v/v*). For the conventional extraction method, a portion of the prepared samples was left to stand for 24 h at room temperature with occasional stirring. UAE was performed immediately after mixing the milled hazelnut shells with the solvent, using a direct-immersion ultrasonic probe system (Bandelin HD 2000.2, Berlin, Germany; probe diameter 13 mm, nominal power 200 W, frequency 30 kHz) in continuous mode. The UAE parameters were varied as follows: extraction time 10, 15, and 25 min and amplitude 40 and 60%. During UAE treatments, the temperature change in the extracts was recorded every 60 s using a thermometer (M.E.V. Feller, South Shields, UK), with the results presented in the Supplementary Materials. After both classical extraction and UAE, the extracts were filtered through Whatman filter paper (grade 1, 11 μm), sealed, and stored in a refrigerator (4 °C) until chemical analyses were performed.

2.3. Determination of Total Polyphenolic Compounds of Hazelnut Kernel and Shell

The analysis of phenolic compounds included the determination of total phenolic content (TPC), total flavonoid content (TFC), and total non-flavonoid content (TNFC). For the extraction of polyphenolic compounds from hazelnut kernels and shells, $10 \text{ g} \pm 0.01$ of each sample was weighed and homogenized with a total of 100 mL of 80% ethanol.

To improve extraction efficiency, a double sequential extraction with a smaller volume of solvent was performed by boiling the mixture for 10 min under reflux. The resulting extracts were filtered through Whatman filter paper (Ahlstrom Munksjö, Bärenstein, Germany) into 100 mL volumetric flasks, which were then filled to volume with 80% ethanol. TPC, TFC, and TNFC of hazelnut kernel and shell were determined for the extracts described according to Ref. [21]. This method is based on spectrophotometric measurement at 750 nm of the intensity of the blue color formed by the reaction of phenolic compounds with the Folin–Ciocalteu (FC) (BHD Prolabo, Cheshire, UK) reagent (diluted with dH₂O at a 1:2 ratio). To determine TPC, 0.5 mL of extract, 30 mL of dH₂O, 2.5 mL of FC reagent, and 7.5 mL of saturated sodium carbonate solution (Na₂CO₃) were added to a 50 mL volumetric flask and made up to the mark with dH₂O. After 2 h at room temperature, spectrophotometric measurements (1900i, Shimadzu, Kyoto, Japan) were performed using dH₂O as a blank. To determine TNFC, 10 mL of extract, 5 mL of HCl solution (1:4), and 5 mL of formaldehyde were mixed in a 25 mL flask and purged with nitrogen. After 24 h at room temperature in the dark, the samples were filtered through Whatman filter paper and subjected to reaction with FC reagent, as for total phenolics. The TFC was determined from the difference between total phenolics and non-flavonoids. Gallic acid was used as an external standard for TPC, while for TFC, the catechol and results are expressed as mg gallic acid/catechin equivalents per 100 g of fresh weight (mg GAE/100 g FW; mg CHT/100 g FW).

2.4. Determination of Total Polyphenolic Compounds of Hazelnut Shell Extracts

The determination of TPC, TNFC, and TFC of hazelnut shell extracts was performed following the procedure previously described for hazelnut kernels and shells, with appropriate modifications for extract volume and reagent proportions [22]. Briefly, 1 mL of extract and 1 mL of FC reagent (previously diluted with dH₂O at a 1:2 ratio) were mixed in 50 mL volumetric flasks. After a few minutes, 3 mL of saturated Na₂CO₃ solution was added, and the flasks were filled to volume with dH₂O. After 2 h at room temperature, absorbance was measured at 750 nm. Distilled water served as the blank. The total flavonoid content (TFC) of the shell extracts was determined using a modified method [23]. In a 25 mL volumetric flask, 1 mL of extract, 1 mL of 20% HCl (*v/v*), and 0.5 mL of formaldehyde were mixed, and the samples were purged with nitrogen. After 24 h of incubation in the dark at room temperature, samples were filtered through Whatman filter paper, and the FC reaction was carried out as described for TPC. Gallic acid was used as the external standard for TPC (mg GAE/100 g FW) and catechin as the external standard for TFC (mg CHT/100 g FW), and TNFC was calculated as the difference between TPC and TFC.

2.5. Determination of Individual Polyphenolic Compounds

Individual polyphenolic compounds were determined in hazelnut kernels and shells, as well as in conventional and UAE hazelnut shell extracts, using a high-performance liquid chromatography system (LC Nexera, Shimadzu, Kyoto, Japan) equipped with a diode array detector (DAD), as described by Ref. [24]. Ten phenolic compounds were analyzed: chlorogenic acid, ferulic acid, protocatechuic acid, rosmarinic acid, vanillic acid, kaempferol, naringin, quercetin, quercetin-3-glucoside, and rutin trihydrate. Separation was achieved on a C18 column (250 × 4.6 mm, 5 µm; Macherey-Nagel, GmbH, Düren, Germany) maintained at 25 °C. The mobile phase consisted of solvent A (water with 3% formic acid) and solvent B (acetonitrile with 3% formic acid), with gradient elution over 45 min at a flow rate of 0.9 mL/min. The injection volume was 20 µL. Detection wavelengths ranged from 220 to 360 nm, depending on the phenolic compound class. Identification was based on retention times and ultraviolet (UV) spectra compared with those of com-

mercial standards, and quantification was performed using external calibration curves (Table 1) prepared from serial dilutions of each phenolic standard. Results are expressed as mg/100 g fresh weight.

Table 1. Calibration curve equations and R^2 values of analyzed individual phenolic compounds.

Phenolic Compound	Equation	R^2
Chlorogenic acid	$y = 14,511.7x - 66,325.3$	0.9998
Ferulic acid	$y = 27,461.5x - 90,059.3$	0.987
Protocatechuic acid	$y = 90,775.3x - 595,177$	0.9997
Rosmarinic acid	$y = 35,491.8x - 47,825.6$	0.9997
Vanillic acid	$y = 65,980.1x + 143,637$	0.9999
Kaempferol	$y = 88,470.8x - 1,047,410$	0.9998
Naringin	$y = 3941.28x - 30,329.7$	0.9829
Quercetin	$y = 111,886x - 377,503$	0.9999
Quercetin-3-glucoside	$y = 50,449x - 342,648$	0.9997
Rutin trihydrate	$y = 34,107.6x - 238,617$	0.999

2.6. Determination of Antioxidant Capacity

The antioxidant capacity of the extracts was determined spectrophotometrically (Shimadzu 1900i, Kyoto, Japan) using the ABTS (2,2-azinobis (3-ethylbenzothiazoline-6-sulfonic acid)), DPPH (1,1-diphenyl-2-picrylhydrazyl), and FRAP (ferric reducing antioxidant power) assays. The same procedures were applied to all extracts. For the ABTS assay, the $ABTS^{\bullet+}$ radical cation was generated by reacting 7 mM ABTS with potassium persulfate and allowing the mixture to stand in the dark overnight. Before use, the solution was diluted with 96% EtOH to an absorbance of 0.70 ± 0.02 at 734 nm. Then, 160 μ L of hazelnut extract was mixed with 2000 μ L of $ABTS^{\bullet+}$ solution and incubated for 3 min at room temperature, and absorbance was measured at 734 nm. The DPPH radical scavenging activity was determined using a 0.1 mM DPPH solution in 80% EtOH (*v/v*). A 100 μ L aliquot of hazelnut extract was mixed with 1900 μ L of DPPH solution and incubated for 20 min in the dark at room temperature. The decrease in absorbance was then measured at 517 nm. The ferric reducing antioxidant power (FRAP) assay was performed using a freshly prepared FRAP reagent consisting of 300 mM acetate buffer (pH 3.6), 10 mM 2,4,6-Tripyridyl-S-triazine (TPTZ) in 40 mM HCl, and 20 mM $FeCl_3 \cdot 6H_2O$ (10:1:1, *v/v/v*). The reaction mixture contained 80 μ L of sample extract, 720 μ L of dH_2O , and 6240 μ L of FRAP reagent. The mixture was incubated at 37 °C for 5 min, after which absorbance was measured at 593 nm. For all three assays, Trolox was used as the standard for calibration curves, and antioxidant capacity was expressed as mmol Trolox equivalents per liter of extract (mmol TE/L).

2.7. Calculation of Theoretical and Recoverable Total Phenolic Content (TPC)

The theoretical total phenolic content (TPC) present in the shell fraction of hazelnut was calculated based on the measured TPC of the shell and the proportion of shells in the fresh fruit, following the general mass-balance approach for bioactive compound recovery from plant by-products as commonly applied in biomass valorization and green extraction frameworks [25–27].

The calculations were performed as follows:

Shell fraction (f_{shell}):

$$f_{\text{shell}} = \frac{\text{mass of shell}}{\text{mass of fresh fruit}} \quad (1)$$

In this study, the shell fraction was 58% for the ‘Rimski’ variety and 59% for the ‘Istarski duguljasti’ variety.

Theoretical TPC in the shell per kg of fresh fruit was calculated as follows according to [4,9]:

$$\text{TPC}_{\text{theoretical}} = f_{\text{shell}} \times \text{TPC}_{\text{measured}} \quad (2)$$

where $\text{TPC}_{\text{measured}}$ is the total phenolic content of the shell determined experimentally (mg GAE/100 g fresh weight). For conventional extraction with 80% ethanol, $\text{TPC}_{\text{measured}}$ was 292.7 mg GAE/100 g FW; for UAE with 80% ethanol at 60% amplitude and 25 min, $\text{TPC}_{\text{measured}}$ was 521.0 mg GAE/100 g FW.

Recoverable TPC based on extraction efficiency was calculated according to the following expression:

$$\text{TPC}_{\text{recovered}} = \text{TPC}_{\text{theoretical}} \times \frac{r}{100} \quad (3)$$

where r is the extraction recovery rate (%), representing the proportion of phenolic compounds that can be effectively extracted from the shell under given processing conditions [28]. The selected recovery rates (30%, 40%, 50%, 60%, and 70%) represent typical extraction efficiencies reported in the literature for phenolic compounds obtained from various plant matrices using conventional and green extraction techniques [29]. These rates were chosen to cover a realistic range of recoverable TPC, allowing comparison between conventional and UAE methods and to provide practical information for potential industrial valorization of hazelnut shells. This approach is consistent with sustainable biomass valorization concepts, where the assessment of both theoretical availability and practical recoverability of bioactive compounds is considered essential for evaluating process efficiency and environmental performance.

2.8. Statistical Analysis

All extraction procedures and chemical analyses were performed in triplicate ($n = 3$), and results are expressed as mean values $\pm$ standard deviation. Statistical analysis of data was conducted in R environment v4.5.1 (R Core Team, 2025). In the first stage, a two-way ANOVA was performed to evaluate the effects of variety ('Rimski' vs. 'Istarski duguljasti') and tissue type (shell vs. kernel) on the yield of TPC, TFC, TNFC, and eleven individual phenolic compounds, as well as on the antioxidant capacity measured by three methods (ABTS, DPPH, and FRAP). When significant main effects or interactions were detected, pairwise comparisons were conducted using Tukey's Honest Significant Difference (HSD) test.

In the second stage, the influence of extraction type and conditions on the yield of phenolic compounds and the antioxidant capacity of hazelnut shells was analyzed using one-way ANOVA. Statistically significant differences between extraction methods were determined by performing Tukey's HSD test.

Correlations between antioxidant capacity methods and yields of phenolic compounds were assessed using Pearson correlation coefficients and visualized in the form of a circo diagram using package circlize v0.4.16 [29].

3. Results and Discussion

3.1. Shells vs. Kernels

Figure 1 presents the results of the total polyphenolic content (TPC), including total flavonoid content (TFC) and total non-flavonoid content (TNFC), individual polyphenolic compounds, and antioxidant capacity in the shell and kernel of two hazelnut varieties, 'Rimski' and 'Istarski duguljasti'.

'Istarski duguljasti' shell. In both varieties, TFC and TNFC were significantly higher in the shell compared to the kernel, with about 21% higher TFC in the 'Rimski' variety and 37% higher in the 'Istarski' variety, while TNFC was 35% higher in the 'Rimski' variety and up to 75% higher in the 'Istarski duguljasti' shell compared to the kernels. Slight variations were observed in the comparison of individual flavonoid compounds between shell and kernel, although most analyzed compounds were more abundant in the kernel than in the shell. Statistical differences were recorded for all analyzed individual flavonoid compounds, except for quercetin 3-glucoside and kaempferol, when considering the nut part and the interaction between variety and part ($V \times P$). For example, the highest contents of rutin trihydrate, quercetin, and naringin were recorded in the kernel, particularly in the 'Istarski duguljasti' variety. Among the individual non-flavonoid compounds analyzed, only gallic acid showed higher values in the shell compared to the kernel. Other compounds, including protocatechuic, chlorogenic, vanillic, ferulic, and rosmarinic acids, were higher in the kernel than in the shell, and when comparing varieties, their contents were mostly higher in the 'Istarski duguljasti' variety. Although the present study did not aim to statistically compare hazelnut cultivars, the observed differences between 'Rimski' and 'Istarski duguljasti' shells may be partly attributed to varietal characteristics such as shell thickness, anatomical structure, and lignin content [31–33]. Previous studies have shown that lignin-rich matrices can retain phenolic compounds through covalent and non-covalent interactions, affecting their extractability [34]. In addition, environmental factors and growing conditions are known to influence phenolic biosynthesis in hazelnuts, which may further contribute to the observed variability [32]. For antioxidant capacity, significant differences were observed between varieties in all tested assays. However, for the ABTS assay, no significant differences were recorded based on nut part (kernel and shell) or the interaction between variety and part ($V \times P$). The highest antioxidant capacity determined by the ABTS method was observed in the 'Rimski' variety, while no significant differences were found between kernel and shell. Antioxidant capacity values determined by the DPPH assay showed significant differences in the interaction of the tested variables, with the highest value recorded for the kernel of the 'Rimski' variety and the lowest for the kernel of the 'Istarski duguljasti' variety. The FRAP method revealed clearer trends, with the highest antioxidant capacity recorded in the shell of both analyzed hazelnut varieties.

The obtained results indicate that the hazelnut shell is a considerably richer source of total polyphenols compared to the kernel, particularly in the case of the 'Rimski' variety, which exhibited almost twice higher TPC values than 'Istarski duguljasti'. Hazelnut shells are commonly regarded as a by-product of the nut industry but are known to contain substantial amounts of phenolic acids, flavonoids, and tannins, contributing to high antioxidant capacity [6]. They have been described as a promising source of bioactive compounds with potential prebiotic and functional properties, highlighting the importance of their extraction and valorization [5]. Hazelnut shells are particularly rich in phenolic compounds such as gallic, protocatechuic, and syringic acids, as well as catechin derivatives [4]. Quantitatively, the TPC values obtained in this study are generally consistent with those reported in the literature, although methodological differences such as solvent type, extraction time, and particle size can influence the absolute values. For example, Di Michele et al. [4] reported TPC values for hazelnut shell extracts in the range of approximately 1.3–4.7 mg GAE/g extract depending on extraction conditions. Similarly, Yuan et al. [9] observed TPC values in the range of about 3.5–12 mg GAE/g extract for hazelnut shell phenolics under optimized extraction conditions. The slightly higher TPC values seen in our UAE treatments may be attributed to enhanced mass transfer and improved cell wall disruption under ultrasonic conditions, in addition to differences in cultivar and extraction parameters. Therefore, the higher TPC observed in the shell compared to the kernel in both analyzed varieties is

consistent with the literature data. The variability between 'Rimski' and 'Istarski duguljasti' shells could be attributed to genotypic differences, environmental conditions, and potential differences in shell thickness or lignification degree, which are known to influence the accumulation of polyphenolic compounds. Shells with a higher degree of lignification tend to accumulate greater amounts of polyphenols, as lignin deposition correlates with increased shell thickness and contributes to the formation of protective barriers influencing cell differentiation and defense responses [29,35]. Moreover, the higher content of protocatechuic, chlorogenic, vanillic, ferulic, and rosmarinic acids in the kernel compared to the shell is expected considering the distinct structural and biochemical composition of these tissues. The kernel, being a metabolically active tissue rich in proteins, lipids, and amino acids, contains higher levels of soluble phenolic acids such as protocatechuic, chlorogenic, vanillic, ferulic, and rosmarinic acids [36,37]. These compounds are often associated with primary metabolism and antioxidant protection of the cellular contents. In contrast, the shell is a lignocellulosic, highly polymerized structure mainly composed of lignin, cellulose, and hemicellulose. Its phenolic profile is therefore dominated by structural phenolics, particularly simple phenolic acids such as gallic acid, which are typically bound to lignin. The higher gallic acid content in the shell reflects its role in providing rigidity and oxidative stability to the cell wall matrix [15,38]. Regarding the antioxidant capacity, it is important to emphasize that all applied methods showed very high values for both the shell and the kernel, although statistically significant differences between them (for both the 'Rimski' and 'Istarski duguljasti' varieties) were observed only with the FRAP method. These results are expected, considering that the FRAP method is more sensitive to hydrophilic antioxidants, which dominate in the hazelnut shell. The obtained results are also consistent with previous studies confirming the high antioxidant potential of both the shell and the kernel of hazelnuts [3,6,39]. In contrast, the ABTS and DPPH methods show sensitivity toward lipophilic components as well. Specifically, the ABTS method responds to both hydrophilic and lipophilic compounds [40], and although no statistically significant differences between the shell and the kernel were detected for either 'Rimski' or 'Istarski duguljasti', a trend of slightly higher antioxidant capacity values was observed for the shell. On the other hand, the DPPH method, which is primarily sensitive to lipophilic antioxidants [40], showed expectedly higher antioxidant capacity values in the kernel compared to the shell, in line with the fact that the hazelnut kernel predominantly contains lipid components. It should also be considered that the lipid-rich matrix of the hazelnut kernel may influence the accuracy of antioxidant capacity determination. High oil content and the presence of fatty acids can affect the solubility, accessibility, and reactivity of antioxidant compounds, particularly in assays based on radical scavenging mechanisms such as ABTS and DPPH. In addition, trace elements naturally present in the kernel may participate in redox reactions, potentially modulating the measured antioxidant response, especially in the FRAP assay. Therefore, differences in antioxidant capacity between the shell and the kernel should be interpreted not only in terms of antioxidant composition but also in relation to matrix effects. Overall, these results support the growing body of evidence that hazelnut shells represent a valuable source of natural antioxidants and should be considered for further valorization within circular bioeconomy frameworks, as demonstrated by Di Michele et al. [4], who highlighted the recovery of bioactive compounds from hazelnut shells for high-value applications, and further supported by Aguado-González et al. [41], who emphasized cascade valorization strategies of hazelnut industry by-products, integrating antioxidant recovery with sustainable industrial applications.

3.2. Extraction Technologies for Polyphenol Recovery from Hazelnut Shells

For the purpose of valorizing hazelnut shells as a potential source of bioactive polyphenolic compounds, a simultaneous comparison of conventional solid–liquid extraction and ultrasound-assisted extraction (UAE) was conducted to evaluate the recovery potential of these compounds. The aim was to explore the feasibility of obtaining phenolic-rich extracts from hazelnut shells for potential application in high value-added products in the pharmaceutical, food, cosmetic, and medical industries. The extraction results for both conventional and UAE of the ‘Rimski’ hazelnut shell are presented in Figure 2. The data clearly indicate a pronounced positive effect of UAE on the yield of polyphenolic compounds (Table S1). Significantly higher total phenolic content (TPC), total flavonoid content (TFC), and total non-flavonoid content (TNFC) were recorded in UAE treatments compared to conventional extraction ($p \leq 0.0001$). For instance, under UAE conditions (80% ethanol, 60% amplitude, and 25 min), TPC was 78% higher than that obtained by conventional extraction with the same solvent. Similarly, the highest TFC value under these UAE settings was nearly twice as high as in conventional extraction, while TNFC was approximately 75% higher. A similar trend was observed for individual phenolic compounds analyzed by HPLC. The most abundant compounds across all treatments were naringin, kaempferol, rutin trihydrate, protocatechuic acid, and gallic acid, while quercetin 3-glucoside, ferulic, vanillic, and rosmarinic acids were present in lower concentrations. UAE treatments, particularly those with higher amplitude and longer extraction time, resulted in increased concentrations of most phenolic acids. For example, naringin content around 58% higher than in conventional extraction, indicating more efficient release of phenolic compounds from the cellular structures of the shell under ultrasonic treatment.

The effect of ethanol concentration (50% and 80% *v/v*) on extraction efficiency was also evaluated in both methods. In conventional extraction, 50% ethanol yielded higher TPC and TNFC values compared to 80% ethanol (TPC ~8% higher, TNFC ~11% higher). In UAE, besides ethanol concentration, other factors such as amplitude and extraction time were varied simultaneously, making it difficult to isolate the individual effect of ethanol concentration. More specifically, using 50% ethanol in UAE, the highest TPC yield was obtained at 60% amplitude and 25 min extraction. Compared to the same UAE settings with 80% ethanol, this value was approximately 14% lower. However, this trend was not consistent across other amplitude and extraction time combinations, suggesting that the synergistic effect of specific parameters, rather than individual factors, is key to maximizing extraction yield. The effect of UAE on individual polyphenolic compounds was not uniformly higher under 80% ethanol, 60% amplitude, and 25 min. Most compounds, including rutin trihydrate, naringin, kaempferol, gallic acid, and protocatechuic acid, showed higher contents under these UAE conditions compared to conventional extraction with 80% ethanol, whereas certain compounds, such as quercetin and vanillic acid, reached their highest concentrations under conventional extraction with 50% ethanol.

Analysis of the antioxidant capacity of the extracts (ABTS, DPPH, and FRAP assays) confirmed the positive effect of UAE on overall antioxidant activity. The highest ABTS and FRAP capacities were recorded under extraction conditions using 80% ethanol, 60% amplitude, and 25 min duration and were 20–40% higher than those obtained by conventional extraction. The increase in FRAP values was particularly pronounced, reaching 3.064 mmol TE/L under optimal UAE conditions, representing an increase of almost 80% compared to the conventional procedure.

type of extraction	conventional		UAE												min max
ethanol concentration (%)	50	80	50						80						
amplitude (%)	-	-	40			60			40			60			
time	24 h	24 h	10 min	15 min	25 min	10 min	15 min	25 min	10 min	15 min	25 min	10 min	15 min	25 min	
TPC (mg GAE/100 g)	c	a	bc	d	e	f	dg	h	b	g	i	bc	j	k	291.401 – 522.756
TFC (mg CHT/100 g)	a	a	b	a	c	a	cd	e	cd	e	f	d	f	g	39.187 – 93.071
rutin trihydrate (mg/100 g)	e	a	b	bc	d	bc	ce	d	a	f	g	h	i	j	7.003 – 7.226
quercetin-3-glucoside (mg/100 g)	b	a	b	b	b	b	b	b	a	a	ab	a	ab	b	6.809 – 7.076
quercetin (mg/100 g)	g	ab	cd	cd	cd	cd	acd	acd	c	abd	e	abcd	b	f	3.381 – 3.481
naringin (mg/100 g)	l	a	b	c	d	e	f	g	a	c	h	i	j	k	10.074 – 16.04
kaempferol (mg/100 g)	d	ab	cd	abc	ab	ac	ab	ab	ab	ef	e	bf	ef	g	11.825 – 11.909
TNFC (mg GAE/100 g)	be	a	b	c	d	e	f	g	a	h	g	a	d	i	244.611 – 430.242
gallic acid (mg/100 g)	ac	abc	a	a	bc	a	abc	b	abc	ac	d	abc	b	d	2.34 – 4.088
protocatechuic acid (mg/100 g)	abe	abcd	ae	abe	bcd	abe	abcd	cdf	e	abc	df	ab	cdf	f	7.538 – 8.484
chlorogenic acid (mg/100 g)	a	a	bcd	bcde	abe	ae	cd	bcd	cd	bcde	c	bde	bcd	bcde	4.658 – 5.166
vanillic acid (mg/100 g)	c	a	b	c	d	e	b	c	f	g	ab	h	g	de	0.887 – 1.901
ferulic acid (mg/100 g)	bc	ab	c	c	c	c	c	c	a	a	abc	a	abc	c	3.309 – 3.802
rosmarinic acid (mg/100 g)	ac	ab	c	c	c	c	ac	b	c	ac	d	c	c	c	1.38 – 1.603
ABTS (mmol TE/L)	a	a	b	b	b	cd	bc	b	ad	a	ad	ad	ad	acd	2.395 – 2.536
DPPH (mmol TE/L)	h	ab	c	d	a	c	d	bd	ae	f	g	eh	fg	g	0.523 – 0.780
FRAP (mmol TE/L)	d	a	a	b	c	d	e	f	b	ce	g	h	g	i	1.703 – 3.101

Figure 2. Statistical comparison and concentration ranges of total and individual polyphenols and antioxidant capacities in conventional and UAE extracts of ‘Rimski’ hazelnut shells. Cell color intensity indicates relative concentration, with white representing lower and dark blue representing higher values for each variable. Total and individual polyphenolic contents and antioxidant capacities of conventional and UAE extracts of the shells of the ‘Rimski’ hazelnut variety. Extracts denoted by the same letter are not significantly different at $p < 0.05$.

A similar effect of extraction method (conventional vs. UAE) on polyphenolic content was observed for the shell extracts of the ‘Istarski duguljasti’ hazelnut variety (Figure 3, Table S2). In general, lower values of all phenolic compounds were found in the shell extracts of ‘Istarski duguljasti’ compared to ‘Rimski’, which was expected given the higher initial TPC and larger proportion of polyphenols in the shells of the ‘Rimski’ variety. It should be noted that, although the UAE extracts were not further diluted prior to analysis, they were incorporated into the Folin–Ciocalteu reaction mixture in a fixed volume (0.5 mL extract + reagents to 50 mL final volume), ensuring that absorbance measurements were within the linear range of the method. Consequently, the reported TPC values reflect the overall reducing capacity of the extracts rather than an exact sum of individual phenolic compounds, and future studies could explore the effect of varying extract dilution to assess potential matrix effects. Significantly higher values of phenolic compounds (TPC, TFC, and TNFC) were again observed with UAE compared to conventional extraction. On average, the highest TPC values were obtained using UAE at 60% amplitude and 25 min extraction time, with both 50% and 80% ethanol, with no statistically significant difference between these two treatments. These UAE conditions achieved up to 68% higher TPC yield compared to conventional extraction with either 50% or 80% ethanol. Overall, in conventional extraction, no statistically significant difference in TPC yield was observed between 50% and 80% ethanol. Similarly, in UAE at 60% amplitude and 25 min, ethanol

concentration did not significantly affect TPC. These results indicate that, under the tested conditions, ethanol concentration was not a determining factor for extraction efficiency, and UAE parameters (amplitude and extraction time) played a more crucial role. A similar distribution of individual polyphenols as observed in the ‘Rimski’ variety was also found in the extracts of the ‘Istarski duguljasti’ variety during UAE treatment. Once again, naringin and kaempferol were the dominant polyphenols, with their highest concentrations obtained under UAE conditions using 80% ethanol, 60% amplitude, and 25 min extraction time. For example, the naringin content was approximately 53% higher under these UAE conditions compared to conventional extraction with the same solvent concentration.

type of extraction	conventional		UAE												minmax
ethanol concentration (%)	50	80	50						80						
amplitude (%)	-	-	40			60			40			60			
time	24 h	24 h	10 min	15 min	25 min	10 min	15 min	25 min	10 min	15 min	25 min	10 min	15 min	25 min	
TPC (mg GAE/100 g)	a	a	b	c	d	e	e	f	g	h	i	i	j	f	218.146 – 374.537
TFC (mg CHT/100 g)	b	a	b	a	c	a	c	d	c	d	e	f	g	h	33.439 – 85.022
rutin trihydrate (mg/100 g)	df	abc	abc	d	e	adf	g	e	h	b	abcf	bc	acf	dg	7.017 – 7.109
quercetin-3-glucoside (mg/100 g)	abc	ab	abc	abc	abc	abc	abc	c	ab	a	a	bc	a	a	6.217 – 7.07
quercetin (mg/100 g)	h	a	bc	bcd	e	d	b	e	cd	e	f	e	a	g	3.381 – 3.462
naringin (mg/100 g)	n	a	b	c	d	e	f	g	h	i	j	k	l	m	10.374 – 16.911
kaempferol (mg/100 g)	ab	ab	ab	ab	ab	a	ab	ab	ab	ab	ab	ab	ab	b	11.74 – 11.93
TNFC (mg GAE/100 g)	j	a	b	c	d	c	e	f	g	g	h	g	i	c	174.339 – 313.797
gallic acid (mg/100 g)	b	a	b	b	b	b	b	cd	c	cd	c	c	de	e	2.184 – 5.007
protocatechuic acid (mg/100 g)	a	abc	ab	abcd	abcde	abcd	abcde	cde	a	de	abcde	abcd	bcde	e	7.635 – 9.283
chlorogenic acid (mg/100 g)	b	ab	ab	abc	ac	abc	cd	cde	abc	cde	ac	cde	de	e	4.582 – 4.726
vanillic acid (mg/100 g)	bch	ab	abc	de	dfg	ceh	f	fg	abc	ab	deh	a	deg	fg	0.926 – 1.971
ferulic acid (mg/100 g)	b	a	b	b	b	b	b	b	ac	cd	cd	acd	d	e	3.217 – 3.789
rosmarinic acid (mg/100 g)	abc	abc	a	a	ab	a	a	ab	ab	ab	ab	c	bc	ab	1.38 – 2.759
ABTS (mmol TE/L)	a	a	bc	bd	d	b	b	b	ac	ac	ac	ac	ac	ac	2.305 – 2.542
DPPH (mmol TE/L)	a	a	bc	d	d	de	de	f	a	b	de	c	e	g	0.417 – 0.641
FRAP (mmol TE/L)	m	a	b	c	d	e	f	g	h	i	j	k	d	l	0.920 – 2.211

Figure 3. Statistical comparison and concentration ranges of total and individual polyphenols and antioxidant capacities in conventional and UAE extracts of ‘Istarski duguljasti’ hazelnut shells. Cell color intensity indicates relative concentration, with white representing lower and dark blue representing higher values for each variable. Extracts denoted by the same letter are not significantly different at $p < 0.05$.

Based on all presented results, for both hazelnut shell varieties ‘Rimski’ and ‘Istarski’, in general, regardless of the specific individual parameters, the UAE method was significantly more effective in polyphenol extraction than the conventional classic method, with pronounced impact when the key UAE factors were varied: amplitude and duration of treatment. Considering the remarkable efficiency of the fundamental phenomenon underlying high-intensity UAE, namely transient cavitation, the obtained results were expected. The cavitation phenomenon causes the disruption of cellular structures, thereby enhancing and facilitating mass transfer of compounds from the plant matrix into the surrounding solvent [12,42]. Moreover, during the UAE process, a gradual increase in

system temperature was recorded (Figures 1 and 2), which is consistent with the literature describing the ultrasonic mechanism, where localized heat release from cavitation collapse enhances diffusion and mass transfer [43,44]. However, since the temperature remained within a range that does not promote thermal degradation of phenolic compounds (max. 78 and 79 °C), its effect can be considered beneficial in improving extraction efficiency [45]. In addition to the cavitation effect itself, ultrasound induces micro-mixing and turbulence within the extraction medium, thereby reducing diffusion limitations and accelerating mass transfer between the solid and liquid phases [46]. This is the main reason for the significantly higher efficiency of the UAE technique compared to other extraction methods, particularly the conventional solid–liquid extraction. The effectiveness of cavitation in the extraction process of polyphenolic compounds is further reflected in the markedly shorter time required to achieve substantially higher yields. Based on the results of this study, significantly higher polyphenol yields were achieved after only 25 min of UAE treatment compared to 24 h of conventional extraction, even when lower amplitudes were applied.

One of the key factors in solid–liquid extraction, whether performed by conventional or advanced techniques such as UAE, is the selection of an appropriate solvent and solid-to-liquid ratio. Regarding the solid-to-liquid ratio applied in this study, the proportion of 1:2.5 (w/v) was selected based on previous research indicating that lower ratios can increase the contact between sample particles and the solvent, thereby enhancing the diffusion rate of phenolic compounds into the solvent. Although the optimal range of ratios for polyphenol extraction from hard plant matrices is usually between 1:5 and 1:8 (w/v) [44,47], lower ratios can also be effective in systems with a high dry matter content and additionally allow for reduced solvent usage, minimizing environmental impact in line with green chemistry principles. According to the principles of sustainable practices and green chemistry, where the protection of human health and the environment is prioritized, preference is given to GRAS (generally recognized as safe) solvents that exert no negative environmental pressure and are non-toxic to humans [48]. Ethanol belongs to this group of GRAS solvents, and the choice of its concentration has a significant effect on extraction efficiency, primarily due to the solubility characteristics of various polyphenolic compounds [16]. Ethanol is a polar solvent, while polyphenolic compounds exhibit varying degrees of polarity, some are highly polar (e.g., phenolic acids), whereas others are moderately or weakly polar (e.g., many flavonoids and particularly aglycones). Therefore, ethanol is often mixed with water, a more polar solvent, to fine-tune the polarity of the extraction medium for optimal solubilization [17]. In general, lower ethanol concentrations (30–50% v/v , where water predominates) result in a more polar solvent system that favors the extraction of polar phenolic acids and glycosylated flavonoids (e.g., quercetin glycosides, rutin, and chlorogenic and gallic acids). Conversely, higher ethanol concentrations (70–90% v/v) produce a less polar medium that enhances the extraction of less polar flavonoid aglycones (e.g., quercetin, kaempferol, naringenin, and apigenin) and flavones/flavonols with more aromatic rings and fewer hydroxyl groups [18]. The results of this study are partially consistent with these observations, showing a generally better effect of higher ethanol concentration (80% v/v) on the yield of rutin, quercetin-3-glucoside, naringenin, and kaempferol. On the other hand, lower ethanol concentration favored the extraction of protocatechuic and chlorogenic acids, although the differences were not pronounced. These findings may be attributed to the combined influence of other extraction parameters (amplitude and extraction time), which, together with ethanol concentration, significantly affected extraction efficiency. It is important to note that recent scientific studies have reported a significantly higher efficiency of NADESs (natural deep eutectic solvents) compared to ethanol and other conventional solvents still predominantly used in solid–liquid extraction. In general, deep eutectic solvents (DESs) represent a sustainable alternative to traditional solvents due

to their biocompatibility, low toxicity, and environmentally friendly nature. For instance, the authors of [7] obtained substantially higher total phenolic content (TPC) yields from hazelnut shell extracts when using NADESs compared to the ethanol/water system, highlighting the potential of such solvents for improving extraction efficiency. These findings further support the consideration of NADES systems in future studies aimed at optimizing phenolic recovery within the framework of green extraction and sustainable chemistry.

Amplitude in UAE determines the amount of energy transmitted into the liquid phase and thereby influences the cavitation phenomenon. A higher amplitude generates more intense cavitation, leading to greater mechanical disruption of cell walls and consequently facilitating the release and increasing the yield of bioactive compounds (e.g., phenolics). However, excessively high amplitudes may cause degradation of sensitive compounds due to localized heating and overly intense mechanical forces [13,19,49]. Therefore, it is crucial to optimize the amplitude to be sufficiently high for efficient extraction, but not to the extent that it causes phenolic degradation or oxidation. It is important to emphasize that the efficiency of UAE is not governed by individual parameters alone but rather by their mutual interaction. Amplitude determines the intensity of ultrasonic energy and the degree of mechanical disruption of the plant tissue, while extraction time defines the duration of that process. Too short a duration may prevent complete diffusion of phenolic compounds, whereas prolonged exposure, especially at higher amplitudes, can result in the degradation of thermolabile compounds [50]. Thus, fine-tuning the relationship between amplitude and extraction time is essential to achieve an optimal balance between phenolic release and compound stability. Based on the results of this study, an amplitude of 60% of the nominal device power (200 W) and an extraction time of 25 min were found to be adequate for achieving higher total polyphenol yields, although some deviations were observed among individual phenolic compounds. In several cases, higher yields were obtained at lower amplitude (40%) and shorter treatment times, which was particularly evident for phenolic acids. Due to their simple aromatic structure and free hydroxyl groups, phenolic acids are more sensitive to temperature and mechanical stress, making them more prone to oxidation and degradation under intense cavitation conditions.

Compared with other green extraction technologies such as microwave-assisted extraction, pressurized liquid extraction, supercritical CO₂ extraction, or NADES-based systems, UAE offers a favorable balance between extraction efficiency, operational simplicity, and scalability. While alternative techniques may provide higher selectivity or solvent-free extracts, UAE remains particularly attractive for lignocellulosic by-products due to its moderate energy demand, compatibility with aqueous ethanol, and potential for industrial implementation [51].

3.3. Correlation Between Polyphenolic Compounds and Antioxidant Capacity

Figure 4 demonstrates the correlation relationships between total polyphenol content (TPC), total flavonoid content (TFC), total non-flavonoid content (TNFC), as well as identified individual polyphenols in both classic and UAE extracts and the three applied antioxidant capacity assays (FRAP, DPPH, and ABTS). Strong positive correlations were observed between TPC and FRAP, TPC and DPPH, TFC and FRAP, TFC and DPPH, as well as between TNFC and DPPH, and TNFC and FRAP. These results are expected, given that the FRAP (ferric reducing antioxidant power) and DPPH (2,2-diphenyl-1-picrylhydrazyl) methods primarily measure electron-donating ability, i.e., the antioxidant capacity of compounds, which is directly related to the presence of hydroxyl groups in phenolic compounds [52].

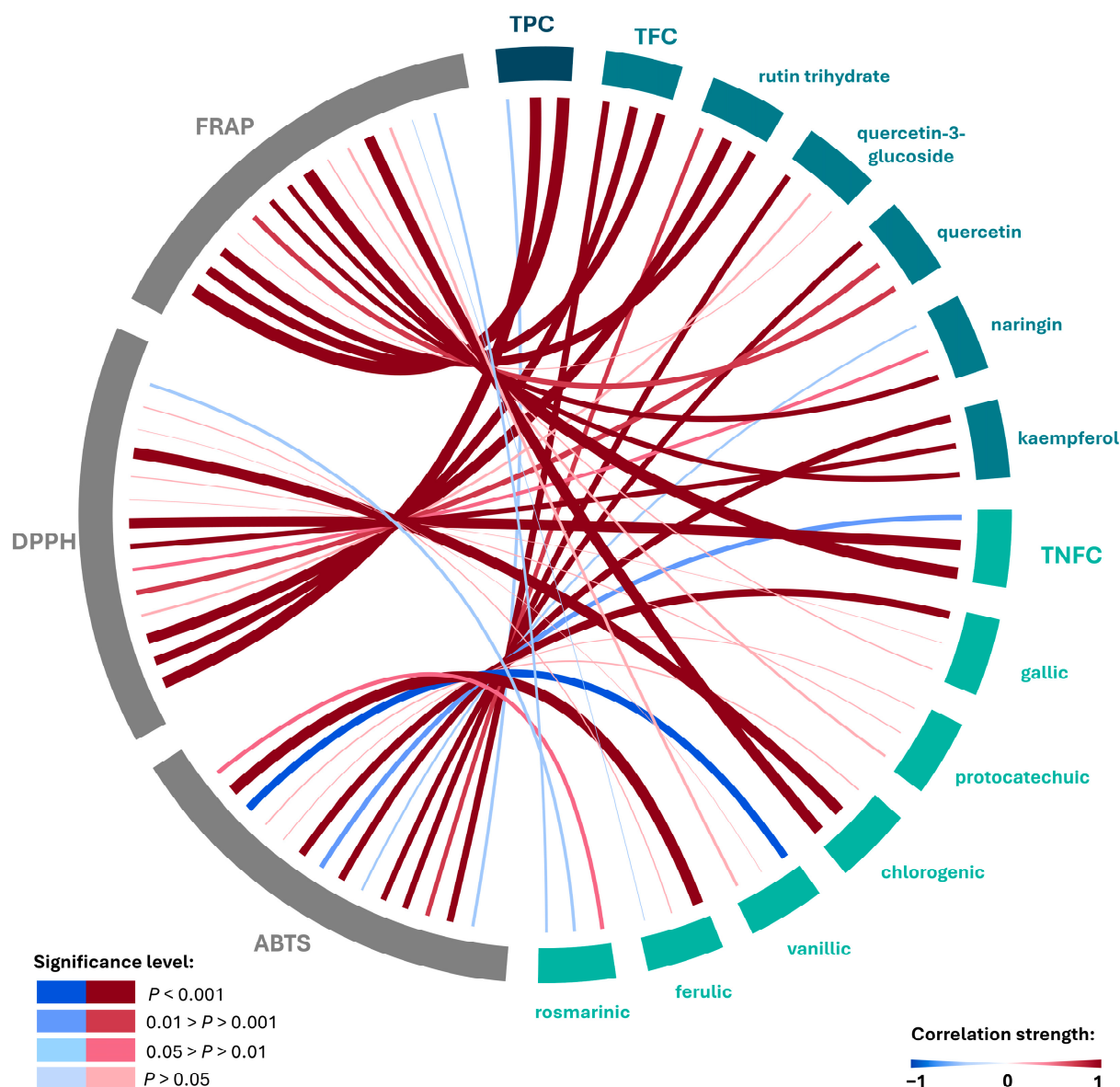


Figure 4. Circos diagram showing Pearson correlation coefficients between three applied antioxidant capacity assays and polyphenolic compounds.

In general, polyphenolic compounds (flavonoids and non-flavonoids) are hydrophilic molecules that act by donating electrons or hydrogen atoms, which is the basis of both methods' mechanisms. Consequently, samples with higher total phenols (TPC), flavonoids (TFC), and non-flavonoid phenols (TNFC) exhibit higher reducing capacity (FRAP) and greater ability to scavenge DPPH radicals. Therefore, positive correlations, where higher phenol content corresponds to higher antioxidant activity, are both expected and common [39]. The ABTS method, on the other hand, also reacts with lipophilic compounds [53], resulting in broader but often weaker correlations with TPC, TFC, and TNFC components. Hence, correlations between TPC/TFC/TNFC and ABTS are generally weaker. An exception is ferulic acid, which shows a strong positive correlation with ABTS, consistent with its chemical structure. Ferulic acid (4-hydroxy-3-methoxycinnamic acid) exhibits amphiphilic properties, acting both hydrophilically and lipophilically due to the presence of both polar and nonpolar functional groups: the phenolic hydroxyl group confers water solubility and antioxidant activity via proton donation, while the methoxy and aromatic groups increase lipophilicity, enhancing interaction with membrane lipids and lipid-soluble radicals [53].

Another polyphenolic compound with amphiphilic properties identified in this study is kaempferol, which exhibits both hydrophilic and lipophilic characteristics owing to its polyhydroxylated yet conjugated aromatic structure [54]. The ABTS assay, which can react with both hydrophilic and lipophilic antioxidants, therefore shows a stronger correlation with kaempferol content. In contrast, the FRAP and DPPH assays, which predominantly assess electron-donating capacity in aqueous systems, show slightly weaker but still strong correlations [55].

Among other determined individual polyphenols, strong positive correlations were also observed between chlorogenic acid and FRAP/DPPH, and positive, though slightly weaker, correlations between rutin trihydrate and FRAP/DPPH. These results are also expected, considering the hydrophilic nature of chlorogenic acid. Chlorogenic acid is a highly hydrophilic polyphenol, an ester of caffeic and quinic acids, containing multiple hydroxyl groups that provide strong electron- and proton-donating ability, explaining its high activity in FRAP and DPPH assays [56,57]. Similarly, rutin trihydrate, a flavonoid glycoside with pronounced hydrophilicity, though with a more complex structure and slightly lower reactivity, still efficiently reduces free radicals in hydrophilic systems, accounting for its positive correlations with FRAP and DPPH. The observed differences in correlations between the antioxidant assays can be explained by the hydrophilic or lipophilic nature of the phenolic compounds: hydrophilic compounds such as chlorogenic acid and rutin trihydrate primarily contribute to DPPH and FRAP activity [58], whereas amphiphilic compounds like ferulic acid and kaempferol interact with lipophilic radicals, resulting in higher ABTS activity [59].

Regarding negative correlations, a pronounced one (indicated by the thick blue line in the graph) was observed between vanillic acid and the ABTS method. This is explainable by the nature of the compound and the potential competitive effects in samples with lower amounts of other, more reactive antioxidants. Vanillic acid exhibits lower radical-scavenging potential, being a monohydroxy derivative of benzoic acid (only one phenolic hydroxyl group and an electron-donating methoxy group) [60,61].

3.4. Recovery of Phenolic Compounds from Hazelnut Shells

The recovery of total phenolic content (TPC) from hazelnut shells of the 'Rimski' variety was evaluated based on the theoretical content calculated from the shell fraction and experimentally determined TPC values for conventional (292.7 mg GAE/100 g) and ultrasound-assisted (521.1 mg GAE/100 g) extraction (UAE). The results were expressed as the amount of phenolics recoverable per kilogram of fresh fruit. Figure 5 illustrates the relationship between recovery rate (30–70%) and the amount of recovered phenolics for both extraction techniques. As expected, the recovered TPC increased proportionally with higher extraction efficiency. UAE consistently yielded higher TPC values compared to conventional extraction across all recovery rates. For instance, at 30% recovery, the amount of phenolics recovered by UAE was approximately 910 mg/kg, nearly twice the amount obtained by conventional extraction (510 mg/kg). At 70% recovery, the difference became more pronounced, reaching 2.11 g/kg (UAE) versus 1.19 g/kg (conventional). These findings indicate the superior efficiency of ultrasound-assisted extraction in enhancing phenolic recovery from hazelnut shells. The observed differences are likely due to the cavitation effect generated by ultrasound waves, which disrupts the plant cell walls and facilitates the release of bound phenolic compounds. Consequently, UAE not only improves extraction yield but also shortens extraction time and may reduce solvent consumption, aligning with sustainable processing goals.

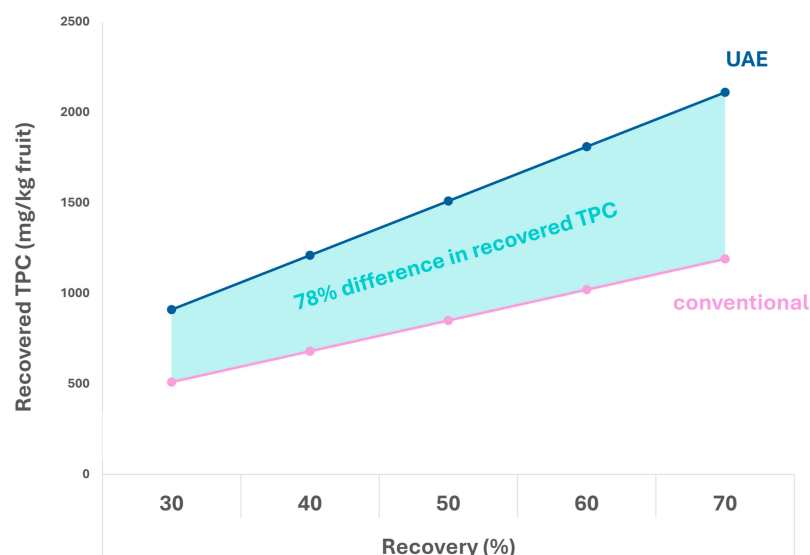


Figure 5. Recovered total phenolic content (TPC) from hazelnut shells using conventional extraction and UAE.

Based on the results obtained in this study, from 58% of hazelnut shells, it is possible to recover approximately 2.11 g/kg of total phenolics (at 70% recovery, UAE). This corresponds to roughly 2.11 kg GAE per tonne of shell waste, representing the active compounds (TPC) that could potentially be utilized by industry. The total phenolic content obtained in this study is consistent with previously reported values for hazelnut shell and other nutshell by-products. Di Michele et al. [4] reported total phenolic contents ranging from approximately 300 to 600 mg GAE/100 g of hazelnut shell, depending on the extraction conditions, which is comparable to the values obtained in the present study, particularly for ultrasound-assisted extraction. Similarly, Yuan et al. [9] reported TPC values in the range of 4–6 g GAE/kg shell using conventional solvent extraction, placing the UAE results obtained here at the upper end of the reported spectrum. More recent studies have demonstrated that green extraction technologies can further enhance phenolic recovery from hazelnut by-products. Elmas et al. [10] showed that ultrasound-assisted, microwave-assisted, and pressurized liquid extraction significantly improve the extraction efficiency compared to conventional techniques, while Bencresciuto et al. [7] reported efficient recovery of bioactive compounds from hazelnut by-products using natural deep eutectic solvents (NADESs). These findings support the suitability of green extraction approaches for lignocellulosic matrices and confirm that the phenolic yields achieved in this study are within, or above, the range reported in the literature. Direct comparison of recovery efficiencies across studies is inherently limited by differences in extraction protocols, solvent systems, and the expression of results; however, the absolute TPC values reported confirm the competitiveness and industrial relevance of the proposed UAE approach. For agro-industrial by-products such as shells, skins, or stems, a recovery of several grams of phenolic compounds per kilogram of fresh material is considered quite good and often commercially attractive, particularly if the extract can be easily concentrated and contains biologically valuable phenolic profiles. It is important to note that UAE extracts of hazelnut shells also contain specific individual polyphenols, with naringin, kaempferol, and protocatechuic acid being particularly abundant. This further emphasizes the significance of shell recovery, especially since these compounds exhibit numerous functional properties and potential health benefits, including antioxidant, antimicrobial, and hepatoprotective activities [62]. Similar phenolic yields have been reported in the literature for other nutshell extracts [7], supporting the potential of these by-products as a source of functional compounds for food,

nutraceutical, or cosmetic applications. Overall, the recovery pattern confirms that the extraction method plays a decisive role in valorizing hazelnut shell by-products as a rich source of bioactive phenolics.

4. Conclusions

Based on the research results, hazelnut shells represent a rich and underutilized source of polyphenolic compounds, with significantly higher total phenolic content (TPC), total flavonoid content (TFC), and total non-flavonoid content (TNFC) compared to kernels in both analyzed varieties ('Rimski' and 'Istarski duguljasti'). The 'Rimski' variety exhibited nearly twice the TPC in both shells and kernels compared to 'Istarski duguljasti', highlighting genotypic influences on polyphenolic accumulation. Flavonoids such as rutin trihydrate, kaempferol, and naringin were predominant in kernels, whereas gallic acid dominated the shell, reflecting differences in tissue structure and composition. Antioxidant capacity, assessed by ABTS, DPPH, and FRAP assays, was high in both kernels and shells, with FRAP showing the most pronounced differences due to its sensitivity to hydrophilic antioxidants. Strong positive correlations between TPC, TFC, TNFC, and FRAP/DPPH confirmed the direct contribution of polyphenols to antioxidant potential. Ultrasound-assisted extraction (UAE) markedly improved the recovery of polyphenolic compounds compared to conventional solid–liquid extraction. Under optimized conditions (80% ethanol, 60% amplitude, and 25 min), TPC increased by up to 78%, TFC nearly doubled, and TNFC rose by ~75%. Individual phenolics, including naringin, kaempferol, rutin trihydrate, protocatechuic acid, and gallic acid, were efficiently recovered, demonstrating UAE's effectiveness in releasing both bound and free compounds. UAE parameters, particularly amplitude and extraction time, were more influential than ethanol concentration in maximizing extraction efficiency. Practically, UAE allowed the recovery of approximately 2.11 g of TPC per kg of hazelnut shell (70% recovery), equivalent to 2.11 kg of GAE per tonne of shell waste, highlighting the potential for industrial valorization. Nevertheless, while large-scale implementation requires further evaluation of energy demand, cost efficiency, and solvent recovery, the relatively mild operating conditions, reduced extraction time, and compatibility with food-grade solvents such as aqueous ethanol suggest that UAE could be feasibly integrated into existing agro-industrial processing lines. These findings confirm that hazelnut shells, often regarded as by-products, can serve as sustainable sources of bioactive polyphenolics for applications in the food, nutraceutical, pharmaceutical, and cosmetic industries. Consequently, shells can also be considered valuable by-products for the production of high value-added products before potential use in green energy generation. This approach fully aligns with the principles of a circular bioeconomy, contributing to reduced environmental pressures and supporting several Sustainable Development Goals, specifically SDG 3, SDG 7, SDG 9, SDG 12, SDG 13, and SDG 15.5.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/chemengineering10020027/s1>, Figure S1. Temperature change (°C) of hazelnut shell alcoholic extracts of the 'Rimski' and 'Istarski duguljasti' varieties during ultrasound-assisted extraction (UAE) at different treatment times (10, 15, and 25 min); Table S1. Total and individual polyphenolic contents and antioxidant capacities of conventional and UAE extracts of the shells of the 'Rimski' hazelnut variety. The values are expressed as averages of triplicates with standard deviation; Table S2. Total and individual polyphenolic contents and antioxidant capacities of conventional and UAE extracts of the shells of the 'Istarski duguljasti' hazelnut variety. The values are expressed as averages of triplicates with standard deviation.

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Abbreviations

The following abbreviations are used in this manuscript:

UAE	Ultrasound-Assisted Extraction
TPC	Total Phenolic Content
TFC	Total Flavonoid Content
TNFC	Total Non-Flavonoid Content
HPLC	High-Performance Liquid Chromatography
FC	Folin–Ciocalteu Reagent
GAE	Gallic Acid
CHT	Catechin
FW	Fresh Weight
DAD	Diode Array Detector
UV	Ultraviolet
ABTS	2,2-azinobis(3-ethylbenzothiazoline-6-sulfonic acid)
DPPH	1,1-diphenyl-2-picrylhydrazyl
FRAP	Ferric Reducing Antioxidant Power
TPTZ	2,4,6-Tripyridyl-S-Triazine
GRAS	Generally Recognized as Safe
NADES	Natural Deep Eutectic Solvent
DES	Deep Eutectic Solvent

References

1. Andika, A.; Perdana, T.; Chaerani, D.; Utomo, D.S. Transitioning towards zero waste in the agri-food supply chain: A review of sustainable circular agri-food supply chain. *Sustain. Futures* **2025**, *10*, 100917. [\[CrossRef\]](#)
2. Rina, R.H. The Waste Management Paradigm Shift from Linear Economy to Circular Economy in Campuses and Urban Communities. *Ecol. Environ. Conserv.* **2022**, *28*, 1316–1323. [\[CrossRef\]](#)
3. Pfeil, J.A.; Zhao, Y.; McGorin, R.J. Chemical composition, phytochemical content, and antioxidant activity of hazelnut (*Corylus avellana* L.) skins from Oregon. *LWT* **2024**, *201*, 116204. [\[CrossRef\]](#)
4. Di Michele, A.; Pagano, C.; Allegrini, A.; Blasi, F.; Cossignani, L.; Raimo, E.D.; Faieta, M.; Oliva, E.; Pittia, P.; Primavilla, S.; et al. Hazelnut shells as source of active ingredients: Extracts preparation and characterization. *Molecules* **2021**, *26*, 6607. [\[CrossRef\]](#) [\[PubMed\]](#)
5. Fusco, A.; Risso, D.; Rosso, G.; Rosso, F.; Manini, F.; Manera, I.; Caligiani, A. Potential valorization of hazelnut shells through extraction, purification and structural characterization of prebiotic compounds: A critical review. *Foods* **2021**, *10*, 1197. [\[CrossRef\]](#) [\[PubMed\]](#)
6. Manterola-Barroso, C.; Padilla Contreras, D.; Ondrasek, G.; Horvatinec, J.; Gavilán CuiCui, G.; Meriño-Gergichevich, C. Hazelnut and walnut nutshell features as emerging added-value byproducts of the nut industry: A review. *Plants* **2024**, *13*, 1034. [\[CrossRef\]](#) [\[PubMed\]](#)

7. Bencresciuto, G.F.; Carnevale, M.; Paris, E.; Gallucci, F.; Santangelo, E.; Migliori, C.A. A Sustainable Alternative for Cosmetic Applications: NADES Extraction of Bioactive Compounds from Hazelnut By-Products. *Sustainability* **2025**, *17*, 1516. [CrossRef]
8. Están, A.; Umaña, M.; Eim, V.S.; Clemente, G.; Simal, S. Conventional and Novel Strategies for Cellulose Isolation from Nut Shells: A Review. *Molecules* **2025**, *30*, 2486. [CrossRef]
9. Yuan, B.; Lu, M.; Eskridge, K.M.; Isom, L.D.; Hanna, M.A. Extraction, identification, and quantification of antioxidant phenolics from hazelnut (*Corylus avellana* L.) shells. *Food Chem.* **2018**, *244*, 7–15. [CrossRef]
10. Elmas, E.; Şen, F.B.; Kublay, İ.Z.; Baş, Y.; Tüfekci, F.; Derman, H.; Bekdeşer, B.; Aşçı, Y.S.; Capanoglu, E.; Bener, M.; et al. Green Extraction of Antioxidants from Hazelnut By-products Using Microwave-Assisted Extraction, Ultrasound-Assisted Extraction, and Pressurized Liquid Extraction. *Food Bioprocess Technol.* **2025**, *18*, 5388–5406. [CrossRef]
11. Kumar, K.; Srivastav, S.; Sharanagat, V.S. Ultrasound assisted extraction (UAE) of bioactive compounds from fruit and vegetable processing by-products: A review. *Ultrason. Sonochem.* **2021**, *70*, 105325. [CrossRef]
12. Islam, M.; Malakar, S.; Rao, M.V.; Kumar, N.; Sahu, J.K. Recent advancement in ultrasound-assisted novel technologies for the extraction of bioactive compounds from herbal plants: A review. *Food Sci. Biotechnol.* **2023**, *32*, 1763–1782. [CrossRef]
13. Shen, L.; Pang, S.; Zhong, M.; Sun, Y.; Qayum, A.; Liu, Y.; Rashid, A.; Xu, B.; Liang, Q.; Ma, H.; et al. A comprehensive review of ultrasonic assisted extraction (UAE) for bioactive components: Principles, advantages, equipment, and combined technologies. *Ultrason. Sonochem.* **2023**, *101*, 106646. [CrossRef] [PubMed]
14. Ong, V.Z.; Wu, T.Y. An application of ultrasonication in lignocellulosic biomass valorisation into bio-energy and bio-based products. *Renew. Sustain. Energy Rev.* **2020**, *132*, 109924. [CrossRef]
15. Xu, Y.; Sismour, E.N.; Parry, J.; Hanna, M.A.; Li, H. Nutritional composition and antioxidant activity in hazelnut shells from US-grown cultivars. *Int. J. Food Sci. Technol.* **2012**, *47*, 940–946. [CrossRef]
16. Pimentel-Moral, S.; Borrás-Linares, I.; Lozano-Sánchez, J.; Alañón, M.E.; Arráez-Román, D.; Segura-Carretero, A. Pressurized GRAS solvents for the green extraction of phenolic compounds from hibiscus sabdariffa calyces. *Food Res. Int.* **2020**, *137*, 109466. [CrossRef] [PubMed]
17. Sharafan, M.; Dziki, A.; Malinowska, M.A.; Sikora, E.; Szopa, A. Targeted Delivery Strategies for Hydrophilic Phytochemicals. *Appl. Sci.* **2025**, *15*, 7101. [CrossRef]
18. Alara, O.R.; Abdurahman, N.H.; Ukaegbu, C.I. Extraction of phenolic compounds: A review. *Curr. Res. Food Sci.* **2021**, *4*, 200–214. [CrossRef]
19. González-Silva, N.; Nolasco-González, Y.; Aguilar-Hernández, G.; Sáyago-Ayerdi, S.G.; Villagrán, Z.; Acosta, J.L.; Montalvo-González, E.; Anaya-Esparza, L.M. Ultrasound-assisted extraction of phenolic compounds from Psidium cattleianum leaves: Optimization using the response surface methodology. *Molecules* **2021**, *27*, 3557. [CrossRef]
20. Croatian Agency for Agriculture and Food. Sortna Lista Voćnih Vrsta. 2025. Available online: <https://www.hapih.hr/wp-content/uploads/2025/09/2.1-Sortna-lista-vocnih-vrsta.pdf> (accessed on 15 November 2025).
21. Ough, C.S.; Amerine, M.A. *Methods for Analysis of Musts and Wines*, 2nd ed; Wiley: Hoboken, NJ, USA, 1988.
22. Shukla, S.; Mehta, A.; Mehta, P.; Bajpai, V.K. Antioxidant ability and total phenolic content of aqueous leaf extract of Stevia rebaudiana Bert. *Exp. Toxicol. Pathol.* **2012**, *64*, 807–811. [CrossRef]
23. Abou-Arab, E.A.; Abu-Salem, F.M. Evaluation of bioactive compounds of Stevia rebaudiana leaves and callus. *J. Food Dairy Sci.* **2010**, *1*, 209–224. [CrossRef]
24. Repajić, M.; Cegledi, E.; Kruk, V.; Pedisić, S.; Çinar, F.; Bursać Kovačević, D.; Žutić, I.; Dragović-Uzelac, V. Accelerated Solvent Extraction as a Green Tool for the Recovery of Polyphenols and Pigments from Wild Nettle Leaves. *Processes* **2020**, *8*, 803. [CrossRef]
25. Saykova, S.; Todorov, D.; Gencheva, R. Mass-balance and recovery analysis of phenolic compounds from plant residues. *J. Chem. Technol. Metall.* **2018**, *53*, 1093–1102.
26. Lameirão, F.; Pinto, D.; Vieira, E.; Peixoto, A.F.; Freitas, V.; Delerue-Matos, C. Green-sustainable recovery of phenolic and antioxidant compounds from agro-industrial by-products. *Antioxidants* **2020**, *9*, 267. [CrossRef]
27. de Souza Mesquita, L.M.; Contieri, L.S.; e Silva, F.A.; Bagini, R.H.; Bragagnolo, F.S.; Strieder, M.M.; Sosa, F.H.; Schaeffer, N.; Freire, M.G.; Ventura, S.P.; et al. Path2Green: Introducing 12 green extraction principles and a novel metric for assessing sustainability in biomass valorization. *Green Chem.* **2024**, *26*, 10087–10106. [CrossRef]
28. Garcia-Mendoza, M.; Rodríguez-Pérez, C.; Segura-Carretero, A.; Fernández-Gutiérrez, A. Recovery of phenolic compounds from plant by-products using green extraction methods: Ultrasound, microwave, and pressurized liquid extraction. *J. Food Eng.* **2021**, *293*, 110397.
29. Gu, Z.; Gu, L.; Eils, R.; Schlesner, M.; Brors, B. circlize Implements and enhances circular visualization in R. *Bioinform.* **2014**, *30*, 2811–2812. [CrossRef]
30. Platzer, M.; Kiese, S.; Herfellner, T.; Schweiggert-Weisz, U.; Eisner, P. How does the phenol structure influence the results of the Folin-Ciocalteu assay? *Antioxidants* **2021**, *10*, 811. [CrossRef]

31. Ozturk, B.; Noyan, H.; Uzun, S.; Karagol, S.; Erdem, H.; Ondin, M. Comparative analysis of phytochemical compounds and quality characteristics during the juvenile stage of hazelnut cultivars from Italy and Türkiye. *BMC Plant Biol.* **2025**, *25*, 1596. [\[CrossRef\]](#)
32. Matin, A.; Brandić, I.; Voća, N.; Bilandžija, N.; Matin, B.; Jurišić, V.; Antonović, A.; Krička, T. Changes in the Properties of Hazelnut Shells Due to Conduction Drying. *Agriculture* **2023**, *13*, 589. [\[CrossRef\]](#)
33. Batelja Lodeta, K.; Očić, V.; Šakić Bobić, B.; Bolarić, S.; Jemrić, T.; Vuković, M.; Benčić, Đ.; Nejašmić, D.; Gadže, J.; Gugić, J.; et al. Bioaktivne komponente i mineralni sastav lješnjaka 'Istarski duguljasti' i 'Rimski'. In Proceedings of the 57. hrvatski i 17. međunarodni simpozij Agronoma, Fakultet agrobiotehničkih znanosti Sveučilišta Josipa Jurja Stross-mayera, Osijek, Croatia, 19–24 June 2022; pp. 554–558.
34. Webber, M.S.; Puente-Urbina, A.; Myers, L.C.; Woodworth, S.P.; Pellerin, E.J.; Jang, J.H.; Bussard, J.R.; Metzger, A.; Donohoe, B.S.; Stone, M.L.; et al. Lignin-Derived Phenolic Compounds and Water Are Effective Cosolvents for Reductive Catalytic Fractionation. *ACS Sustain. Chem. Eng.* **2025**, *13*, 19199–19209. [\[CrossRef\]](#)
35. Okonkwo, C.E.; Hussain, S.Z.; Onyeaka, H.; Adeyanju, A.A.; Nwonuma, C.O.; Bashir, A.A.; Farooq, A.; Zhou, C.; Shittu, T.D. Lignin polyphenol: From biomass to innovative food applications, and influence on gut microflora. *Ind. Crops Prod.* **2023**, *206*, 117696. [\[CrossRef\]](#)
36. Călinoiu, L.F.; Vodnar, D.C. Whole grains and phenolic acids: A review on bioactivity, functionality, health benefits and bioavailability. *Nutrients* **2018**, *10*, 1615. [\[CrossRef\]](#) [\[PubMed\]](#)
37. Kumar, N.; Goel, N. Phenolic acids: Natural versatile molecules with promising therapeutic applications. *Biotechnol. Rep.* **2019**, *24*, 00370. [\[CrossRef\]](#)
38. Shahidi, F.; Hossain, A. Importance of insoluble-bound phenolics to the antioxidant potential is dictated by source material. *Antioxidants* **2023**, *12*, 203. [\[CrossRef\]](#)
39. Gavilán-CuiCui, G.; Padilla-Contreras, D.; Manterola-Barroso, C.; Morina, F.; Meriño-Gergichevich, C. Antioxidant Performance in Hazelnut (*Corylus avellana* L.) Cultivars Shell Is Substantially Influenced by Season and Locality. *Agronomy* **2024**, *14*, 1412. [\[CrossRef\]](#)
40. Munteanu, I.G.; Apetrei, C. Analytical methods used in determining antioxidant activity: A review. *Int. J. Mol. Sci.* **2021**, *22*, 3380. [\[CrossRef\]](#)
41. Aguado-González, L.; Sierra-Pérez, J.; Forte, C.; López-Fornies, I.; Blanc, S. Cascade valorization of hazelnut industry by-products for industrial use through co-creative processes. *J. Clean. Prod.* **2025**, *494*, 144989. [\[CrossRef\]](#)
42. Ponphaiboon, J.; Krongrawa, W.; Aung, W.W.; Chinatangkul, N.; Limmatvapirat, S.; Limmatvapirat, C. Advances in natural product extraction techniques, electrospun fiber fabrication, and the integration of experimental design: A comprehensive review. *Molecules* **2023**, *28*, 5163. [\[CrossRef\]](#)
43. Zhu, X.; Das, R.S.; Bhavya, M.L.; Garcia-Vaquero, M.; Tiwari, B.K. Acoustic cavitation for agri-food applications: Mechanism of action, design of new systems, challenges and strategies for scale-up. *Ultrason. Sonochem.* **2024**, *105*, 106850. [\[CrossRef\]](#)
44. Mungwari, C.P.; King'ondou, C.K.; Sigauke, P.; Obadele, B.A. Conventional and modern techniques for bioactive compounds recovery from plants. *Sci. Afr.* **2025**, *27*, 02509. [\[CrossRef\]](#)
45. Antony, A.; Farid, M. Effect of temperatures on polyphenols during extraction. *Appl. Sci.* **2022**, *12*, 2107. [\[CrossRef\]](#)
46. Chemat, F.; Rombaut, N.; Sicaire, A.G.; Meullemiestre, A.; Fabiano-Tixier, A.S.; Abert-Vian, M. Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. *Ultrason. Sonochem.* **2017**, *34*, 540–560. [\[CrossRef\]](#) [\[PubMed\]](#)
47. Predescu, N.C.; Papuc, C.; Nicorescu, V.; Gajaila, I.U.L.I.A.N.A.; Goran, G.V.; Petcu, C.D.; Stefan, G.E.O.R.G.E.T.A. The influence of solid-to-solvent ratio and extraction method on total phenolic content, flavonoid content and antioxidant properties of some ethanolic plant extracts. *Rev. Chim.* **2016**, *67*, 1922–1927.
48. Food and Drug Administration (FDA). *Substances Generally Recognized as Safe*; Code of Federal Regulations, title 21, part 182; U.S. Government Publishing Office: Washinton, DC, USA, 2003.
49. Lee, Z.J.; Xie, C.; Duan, X.; Ng, K.; Suleria, H.A. Optimization of ultrasonic extraction parameters for the recovery of phenolic compounds in Brown seaweed: Comparison with conventional techniques. *Antioxidants* **2024**, *13*, 409. [\[CrossRef\]](#) [\[PubMed\]](#)
50. Gil-Martín, E.; Forbes-Hernández, T.; Romero, A.; Cinciosi, D.; Giampieri, F.; Battino, M. Influence of the extraction method on the recovery of bioactive phenolic compounds from food industry by-products. *Food Chem.* **2022**, *378*, 131918. [\[CrossRef\]](#) [\[PubMed\]](#)
51. Roobab, U.; Aadil, R.M.; Kurup, S.S.; Maqsood, S. Comparative evaluation of ultrasound-assisted extraction with other green extraction methods for sustainable recycling and processing of date palm bioresources and by-products: A review of recent research. *Ultrason. Sonochem.* **2025**, *114*, 107252. [\[CrossRef\]](#)
52. Shahidi, F.; Zhong, Y. Measurement of antioxidant activity. *J. Funct. Foods* **2015**, *18*, 757–781. [\[CrossRef\]](#)
53. Purushothaman, J.R.; Rizwanullah, M. Ferulic acid: A comprehensive review. *Cureus* **2024**, *16*, e68063. [\[CrossRef\]](#)

54. Chen, J.; Zhong, H.; Huang, Z.; Chen, X.; You, J.; Zou, T. A critical review of kaempferol in intestinal health and diseases. *Antioxidants* **2023**, *12*, 1642. [[CrossRef](#)]
55. Spiegel, M.; Andruniów, T.; Sroka, Z. Flavones' and flavonols' antiradical structure–activity relationship—A quantum chemical study. *Antioxidants* **2020**, *9*, 461. [[CrossRef](#)]
56. Nakanishi, K.; Goto, T.; Itô, S. *Natural Products Chemistry: Volume 1*; Academic Press: London, UK, 2013.
57. Nguyen, V.; Taine, E.G.; Meng, D.; Cui, T.; Tan, W. Chlorogenic acid: A systematic review on the biological functions, mechanistic actions, and therapeutic potentials. *Nutrients* **2024**, *16*, 924. [[CrossRef](#)]
58. Pencreac'h, G.; Lorentz, C.; Ergon, F.; Soultani-Vigneron, S. Production and properties of chlorogenic acid lipophilic esters. *Lipid Technol.* **2012**, *24*, 108–110. [[CrossRef](#)]
59. Tatipamula, V.B.; Kukavica, B. Phenolic compounds as antidiabetic, anti-inflammatory, and anticancer agents and improvement of their bioavailability by liposomes. *Cell Biochem. Funct.* **2021**, *39*, 926–944. [[CrossRef](#)] [[PubMed](#)]
60. Surya, S.; Sampathkumar, P.; Sivasankaran, S.M.; Pethanasamy, M.; Elanchezhian, C.; Deepa, B.; Manoharan, S. Vanillic acid exhibits potent antiproliferative and free radical scavenging effects under in vitro conditions. *Int. J. Nutr. Pharmacol. Neurol. Dis.* **2023**, *13*, 188–198. [[CrossRef](#)]
61. Magiera, A.; Kołodziejczyk-Czepas, J.; Olszewska, M.A. Antioxidant and Anti-Inflammatory Effects of Vanillic Acid in Human Plasma, Human Neutrophils, and Non-Cellular Models in Vitro. *Molecules* **2025**, *30*, 467. [[CrossRef](#)]
62. Rosales, T.K.O.; Fabi, J.P. Valorization of polyphenolic compounds from food industry by-products for application in polysaccharide-based nanoparticles. *Front. Nutr.* **2023**, *10*, 1144677. [[CrossRef](#)]

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