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Mathematical modelling and thermodynamic parameters of total polyphenol extraction using ultrasound in Ilex guayusa Loes

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Mathematical modelling and thermodynamic parameters of total polyphenol extraction using ultrasound in *Ilex guayusa* Loes.

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Abstract

This study investigated the applicability of mathematical models to describe ultrasound-assisted extraction of total phenolic compounds (TPC) from *Ilex guayusa* leaves and determined thermodynamic parameters associated with the extraction process. The effect of temperature (40 to 80 °C) and extraction time (5 to 60 min) on TPC yield was studied. Five non-linear models, including Peleg, Power law, Weibull parabolic diffusion, and Elovich models, were evaluated to determine their accuracy in the extraction process. The results indicated that the highest TPC concentration of 3.88±0.44 g gallic acid equivalent/100 g dry weight was found at 60 min and 80 °C. The Power law model presented the best fit with R^2, adjusted R^2, and predicted R^2 values greater than 0.98, describing a temperature-sensitive nonlinear diffusion kinetics ($n \approx 0.24$-0.28) temperature sensitive. In addition, the mean square deviation, normalised mean square deviation and chi-square statistic values were less than 0.072, 2.126 % and 0.209 %, respectively. The thermodynamic parameters showed that the TPC extraction process was endothermic, spontaneous and controlled by diffusion with activation energy, enthalpy, entropy and Gibbs free energy values of 8.79 kJ/mol, 3.925 kJ/mol, 145.03 J/molK and -47.271 kJ/mol, respectively. The findings provide key information for the design of efficient TPC extraction processes in *I. guayusa*, supporting its industrial application as a sustainable raw material.

Keywords: Extraction kinetics, activation energy, non-linear models, power law.

Introduction

Over recent decades, phenolic compounds have attracted growing scientific interest due to their antioxidant, anti-inflammatory and antimicrobial properties, which make them secondary metabolites of food, cosmetic and therapeutic importance (Sun et al., 2024). These bioactive molecules of plant origin are of relevance to the scientific community due to their potential use in the pharmaceutical, food and cosmetic industries, which has led to the search for efficient methods for their extraction and characterisation (Liu et al., 2023).

Ilex guayusa Loes. is a species native to the Amazon region and widely known for its traditional and ethnomedicinal uses (Gomez-Molina et al., 2024; Rodríguez-Pérez et al., 2019). This Amazonian plant contains a phytochemical matrix rich in phenolic compounds and alkaloids, which give it important bioactive properties (Kelebek et al., 2024). The concentration of polyphenols in its leaves, together with the presence of caffeine, has positioned *I. guayusa* as a promising source of secondary metabolites with potential applications in various industrial sectors (Meneses et al., 2024).

Obtaining polyphenols from plant matrices requires techniques that maximize recovery efficiency while maintaining the structural integrity of the bioactive compounds. In this regard, ultrasound extraction has emerged as an innovative technique that offers significant advantages over conventional extraction techniques such as solvent extraction or maceration (Liu et al., 2022). This technique uses the effects of acoustic cavitation to contribute to cell rupture by increasing mass transfer, which means reduced extraction time, lower solvent consumption and greater selectivity in the recovery of bioactive compounds (Kaltsa et al., 2020; Yusoff et al., 2022).

A comprehensive understanding of extraction processes requires the development of mathematical models that adequately describe mass transfer kinetics and enable the optimisation of operating conditions (Mattos & Zecchi, 2025). Different kinetic models have demonstrated their ability to describe the extraction behaviour of phenolic compounds in plant matrices, providing valuable information on transfer mechanisms and associated kinetic constants (Kinetik et al., 2023; Rebollo-Hernanz et al., 2021; Villamil-Galindo & Piagentini, 2024). These models facilitate the prediction of extraction performance under different experimental conditions and contribute to the design of industrial-scale extraction processes (Rusu et al., 2021).

Despite growing interest in *I. guayusa*, scientific literature lacks comparative studies on mathematical models applied to the extraction of phenolic compounds from its leaves. Previous studies of this species have focused mainly on characterizing its phytochemical composition (Arteaga-Crespo et al., 2020; Chianese et al., 2019; Chóez-Guaranda et al., 2022), leaving a significant gap in our knowledge of the kinetic and thermodynamic aspects of extraction processes. This limitation represents an opportunity to contribute to the understanding of extraction mechanisms in this plant matrix.

On the other hand, thermodynamic parameters such as activation energy, enthalpy, entropy, and Gibbs free energy provide crucial information about the energy viability and spontaneity of extraction processes (Abishli et al., 2021; Silva-Paz et al., 2023). These parameters allow the evaluation of energy barriers associated with mass transfer and the prediction of system behavior under different temperature conditions (Espinoza-Vasquez et al., 2023). However, there are no reports in the scientific literature documenting these thermodynamic parameters for the extraction of polyphenols from *I. guayusa* leaves, limiting a complete understanding of the extraction processes in this species.

The objective of this study was to compare the applicability of five mathematical models to describe the ultrasound-assisted extraction of phenolic compounds from *I. guayusa* leaves,

in order to determine the best model for industrial application. The thermodynamic parameters associated with the process were also determined, thus contributing to scientific knowledge and the development of industrial applications for this species.

Methodology

Materials and reagents

Fresh *I. guayusa* leaves were purchased at the Los Plátanos market in the city of Puyo, Pastaza, Ecuador, in January 2024. The Folin-Ciocalteu reagent, gallic acid, and sodium carbonate (>99% purity) were purchased from Sigma-Aldrich.

Sample preparation

The leaves were dried in a laboratory oven at 40 °C for 48 h. The moisture content of the leaves was 66.48±1.77 % and was determined by weight difference (Gorji et al., 2024). This value was used to express the initial mass on a dry matter basis. The sample was crushed and sieved to obtain particles smaller than 0.5 mm.

Solid-liquid extraction

Extractions were performed at 40, 50, 60, 70, and 80 °C using ultrasonic equipment (brand Wisd.23, model WUC-DO6H). For each temperature, extraction times of 5, 10, 20, 30, 45 and 60 min were applied in order to evaluate different intervals in the extraction curves obtained kinetically. In a glass container, 5 g of the ground plant material was mixed with 100 mL of distilled water and placed in the ultrasonic equipment. The resulting extracts were filtered with Whatman No. 4 paper and analysed immediately after preparation.

Quantification of total polyphenols

The Folin-Ciocalteu colorimetric method was applied according to the procedure described by Arteaga-Crespo et al. (2020). The test was performed using a UV-Vis spectrophotometer (Perkin Elmer brand, Lambda 20 model). In a 10 mL amber volumetric flask, 0.5 mL of aqueous extract was mixed with 0.5 mL of Folin-Ciocalteu reagent. This mixture was left to react for 10 min and then 0.5 mL of 10 % sodium carbonate (Na_2CO_3) was added. The final volume was made up with distilled water and shaken manually for 30 s to ensure complete homogenization of the reagents. After allowing the mixture to stand for 2 h at room temperature, the absorbance was measured at 765 nm using a control solution prepared in the absence of the sample as a blank. The total polyphenol concentration was calculated using a calibration curve prepared with gallic acid (0.2-6 mg/L; $Y=0.0723X+0.0019$; $R^2=0.999$). The results were expressed in grams of gallic acid equivalent per 100 g of dry matter (g GAE/100 g).

Mathematical modelling

The process of extracting total polyphenols was analyzed by adjusting five different kinetic equations, with the aim of identifying the model that best described the experimental behavior. The models evaluated were as follows:

Peleg model

This model is used to describe the kinetics of absorption or extraction in food and biomaterials (Teoh et al., 2024). Equation (1) allows both the initial velocity and the equilibrium of the process to be estimated.

$$C(t) = \frac{t}{k_1 + k_2 \cdot t} \quad (1)$$

Where $C(t)$ is the concentration of total polyphenols as a function of time, k_1 is the rate constant (min g/mg) and k_2 is the capacity constant (g/mg).

Power Law model

This model describes the extraction of an active compound through a solid matrix. The exponent n indicates the transport mechanism. It is useful for processes where the kinetics are non-linear and the extraction does not reach a defined maximum value (Agu & Agulanna, 2020). This model is written as equation (2).

$$C(t) = B \cdot t^n \quad (2)$$

Where $C(t)$ is the total polyphenol concentration, t indicates the extraction time, B is the kinetic constant that depends on temperature, and n is the diffusion exponent.

When deriving the Power-Law model, the extraction rate at any time t can be expressed as equation 3.

$$\frac{dC(t)}{dt} = B \cdot n \cdot t^{n-1} \quad (3)$$

Since the Power-Law model does not yield a rate constant with appropriate units for thermodynamic analysis, the apparent rate constant k was defined as the extraction rate at a fixed reference time, as follows:

$$k = B \cdot n \cdot {t_{ref}}^{n-1} \quad (4)$$

This approach allows obtaining a rate constant with units of concentration per time (g GAE/100g·min).

Weibull model

This model can describe different shapes of extraction curves, adapting to both fast and slow processes. It is useful for modelling extractions assisted by technologies such as microwaves or ultrasound, and allows the kinetics to be adjusted to different experimental conditions (Mahfud et al., 2025). The Weibull model is written as equation (5).

$$C(t) = C \cdot e^{-b \cdot t^m} \quad (5)$$

Where $C(t)$ is the total polyphenol concentration, t indicates the extraction time, C is the initial polyphenol concentration, b is the reaction rate, and m is the value that indicates the shape of the distribution curve.

Parabolic diffusion model

This model assumes that extraction occurs in two stages, first a rapid dissolution stage followed by a diffusion-controlled stage. It is suitable for describing systems where mass transfer by diffusion governs the overall kinetics of the process (John et al., 2024). The extraction of polyphenols can be described by equation (6).

$$C(t) = A_0 + A_1 \cdot \sqrt{t} \quad (6)$$

Where $C(t)$ is the total polyphenol concentration, t is the extraction time, A_0 is the instantaneously recovered extraction, and A_1 is the diffusion constant.

Elovich model

This model is used to describe extraction processes where the rate decreases logarithmically with time. It is useful for heterogeneous systems and processes where the active surface area changes during extraction (Agu & Agulanna, 2020). The relationship between polyphenol concentration and time is expressed as equation (7).

$$C(t) = E_0 + E_1 \cdot ln\,(t) \quad (7)$$

Where $C(t)$ is the total polyphenol concentration, t is the extraction time, E_0 is the initial yield, and E_1 is the initial extraction rate.

Thermodynamic parameters

The parameters of activation energy (Eq. 8), enthalpy and entropy (Eq. 9) and Gibbs free energy (Eq. 10) were determined from experimental values obtained at different temperatures. These parameters allow the sensitivity of the process to temperature changes, the energy required for extraction, and the spontaneity of the system to be characterized.

$$k = A \cdot e^{\left(-\frac{E_a}{RT}\right)} \quad (8)$$

$$log\left(\frac{k}{T}\right) = -log\left(\frac{k_B}{h}\right) + \left(\frac{\Delta S}{2{,}303R}\right) - \left(\frac{\Delta H}{2{,}303RT}\right) \quad (9)$$

$$\Delta G = \Delta H - T\Delta S \quad (10)$$

Where k is the rate constant, A is the pre-exponential factor, (E_a) is the activation energy (kJ/mol), R is the gas constant, T is the absolute temperature, k_B is Boltzmann's constant, h is Planck's constant, ΔS is enthalpy (kJ/mol), ΔH is entropy (kJ/molK), and ΔG is Gibbs free energy (kJ/mol).

Statistical analysis and evaluation of mathematical models

The experiments were expressed as mean value ± standard deviation for n=3. The experimental data were fitted to the mathematical models using Origin 2022 software (trial version). To validate the mathematical models, the coefficients of determination R^2 (Eq. 11), R^2-predicted (Eq. 12), R^2-adjusted (Eq. 13), mean square deviation (Eq. 14), normalized

mean square deviation (Eq. 15) and the chi-square statistic (Eq. 16) were calculated to validate the mathematical models.

$$R^2 = 1 - \sum_{i=1}^{n} \frac{(y_1 - \hat{y}_1)^2}{(y_1 - \bar{y})^2} \quad (11)$$

$$R^2 predicho = 1 - \sum_{i=1}^{n} \frac{\left(y_1 - \widehat{y_{1(-1)}}\right)^2}{(y_1 - \bar{y})^2} \quad (12)$$

$$R^2 ajustado = 1 - (1 - R^2) \cdot \frac{n-1}{n-m-1} \quad (13)$$

$$RMSD = \left(\frac{\sum_{i=1}^{n}(y_i - \hat{y}_i)^2}{n}\right)^{0,5} \quad (14)$$

$$NRMSD = \frac{RMSD}{y_{max} - y_{min}} \quad (15)$$

$$x^2 = \sum_{i=1}^{n} \frac{(y_i - \hat{y}_i)^2}{\hat{y}_i} \quad (16)$$

Where y_1 are the observed values, $\hat{y}_i$ he predicted values, $\bar{y}$ is the mean of the observed values, $y_{i(-i)}$ is the predicted value for data point i, n is the number of observations, and m is the number of variables studied.

Results and discussion

Influence of temperature and extraction time

Increasing the temperature (40 to 80 °C) and time (5 to 60 min) in ultrasound-assisted extraction produced higher yields of total phenolic compounds (TPC) in *I. guayusa* leaves (Figure 1). The concentration obtained at 60 min was 3.13±0.45, 3.27±0.38, 3.40±0.24, 3.62±0.26 and 3.88±0.44 g GAE/100 g dry weight at temperatures of 40, 50, 60, 70 and 80 °C, respectively. These results are consistent with those previously reported in the literature for *I. guayusa*. For example, a content of 3.46 g GAE/100 g has been reported in hydroalcoholic extracts (Arteaga-Crespo et al., 2020). In another study, values of 3.34 g GAE/100 g were found in mature leaves and 2.14 g GAE/100 g in young leaves (Villacís-Chiriboga et al., 2018). Fresh leaves reported a higher value of 5.48 g GAE/100 g (García-Ruiz et al., 2017). Differences in results may be due to various factors, such as plant age, extraction method, solvent type, and environmental conditions. Adult leaves have been shown to have a higher TPC content than young leaves (Villacís-Chiriboga et al., 2018). The extraction technique is another key factor; for example, ultrasound-assisted extraction has demonstrated superior yields compared to traditional techniques such as Soxhlet or maceration (Cadena-Carrera et al., 2019). As for the type of solvent, it has been observed that the use of hydroalcoholic mixtures optimizes TPC extraction, while the exclusive use of ethanol or water can result in lower yields (Cadena-Carrera et al., 2023; Arteaga-Crespo et al., 2020). On the other hand, it has been shown that leaves collected in warm and humid seasons have a higher content of bioactive compounds and antioxidant activity than those

from winter areas. This may be due to water stress and the secondary synthesis experienced by metabolites (Huang et al., 2023; Mwamatope et al., 2021).

Time and temperature during ultrasound-assisted extraction are important variables for maximizing TPC extraction. Ultrasound generates acoustic waves that cause microbubbles to form and collapse in the solvent, a phenomenon known as acoustic cavitation, which is essential for intensifying extraction processes (Zhu et al., 2024). This phenomenon breaks down cell walls and facilitates the release of phenolic compounds trapped in the plant matrix. The increase in temperature reduces the viscosity and surface tension of the solvent, which intensifies cavitation and accelerates the diffusion of bioactive compounds into the liquid medium (Marhamati et al., 2020; Kabudi et al., 2022). Furthermore, longer exposure to ultrasound allows the acoustic waves to act for longer on the plant matrix, promoting cell disruption and tissue fragmentation. This favors mass transfer and facilitates the release of bioactive compounds into the solvent, thus promoting more complete and efficient extraction (Kobus et al., 2021; Liu et al., 2024). On the other hand, various authors have indicated that this process has a limit: if the temperature is too high, polyphenols, which are heat-sensitive compounds, can degrade or oxidise, reducing their yield and quality (Antony & Farid, 2022; Wang et al., 2020). When the temperature is too high, cavitation becomes less efficient because the increase in solvent vapor pressure decreases the intensity of bubble collapse, and the additional thermal energy can break chemical bonds in polyphenols, destroying their structure (Altemimi et al., 2016; Haslina et al., 2021; Marhamati et al., 2020).

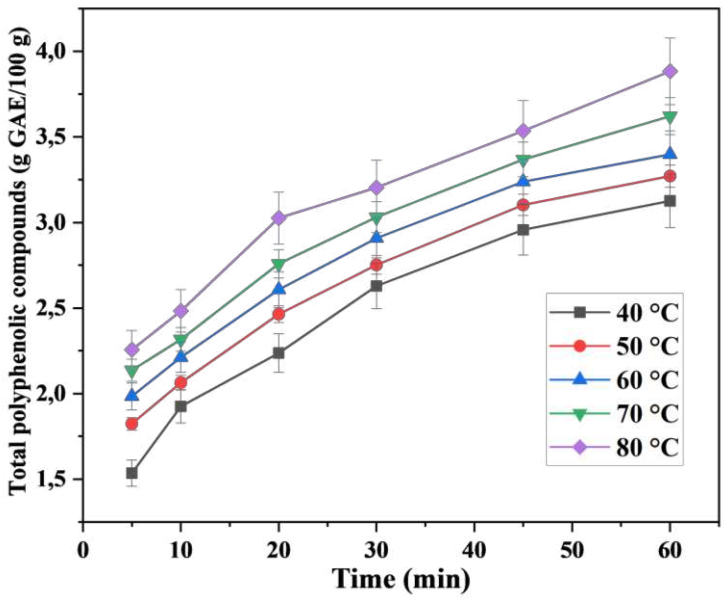


Figure 1. Extraction curves of total polyphenols from dried *I. guayusa* leaves with ultrasound assistance. Concentrations obtained at 40, 50, 60, 70 and 80 °C as a function of time (5 to 60 min).

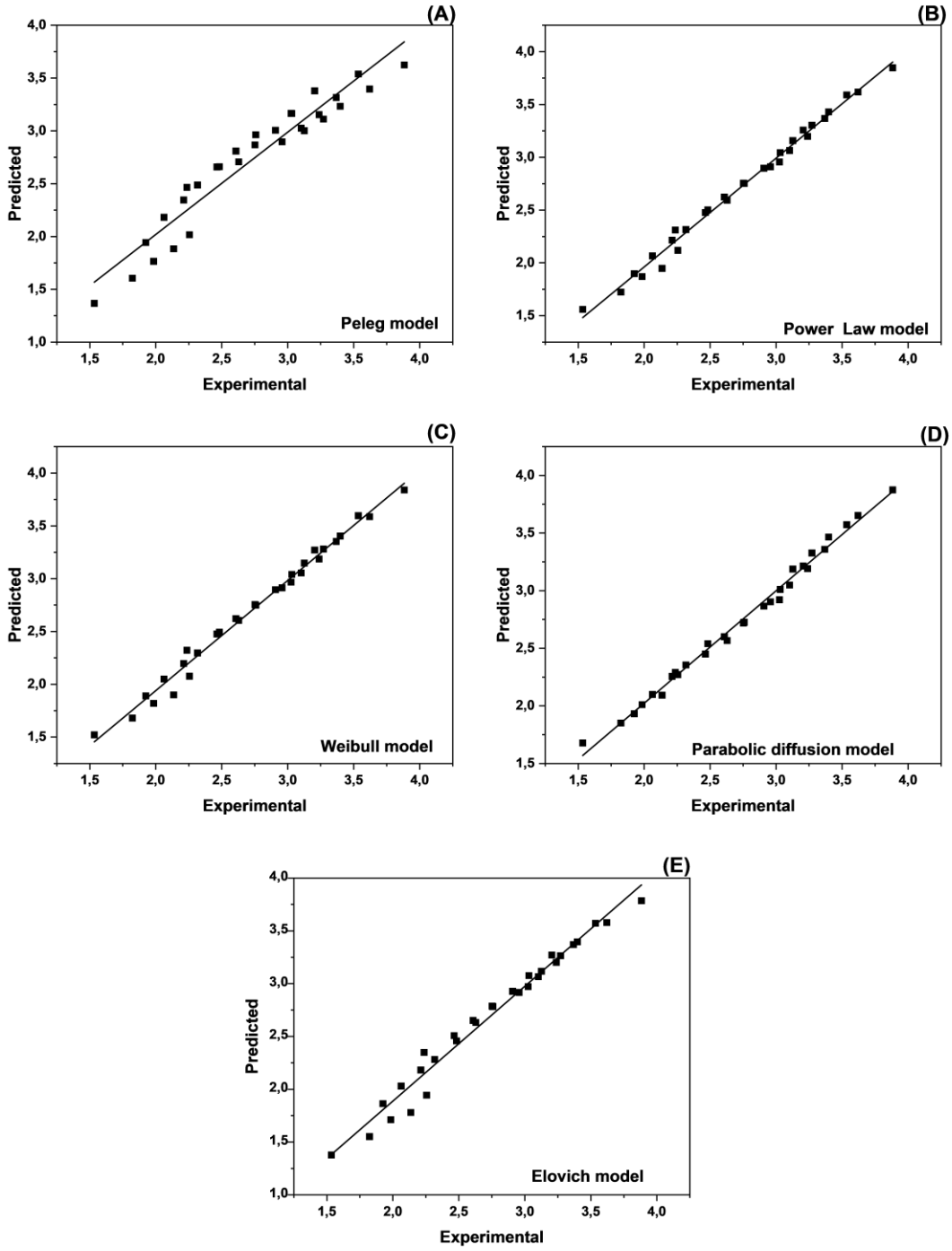
Mathematical modelling

Analysis of the constants of the mathematical models (Table 1) showed how temperature influenced the kinetics and extraction efficiency of total phenolic compounds (TPC) in dried

I. guayusa leaves. In the Peleg model, it was observed that the constants decreased from 2.175 to 1.199 for k_1 and from 0.297 to 0.256 for k_2 when the temperature was increased from 40 °C to 80 °C. This behavior has been reported in the extraction of TPC from curry leaves and grape seeds, where lower values of k_1 and k_2 at elevated temperatures showed faster and more efficient extraction, as these constants are related to the initial rate and maximum extraction capacity, respectively (Bucić-Kojić et al., 2007; Patil et al., 2021). In the Power Law model, the velocity constant B increased from 0.987 to 1.440 with increasing temperature. This increase in B shows that thermal energy improves the extraction rate. On the other hand, the constant n, which represents the extraction mechanism, shows a slight decrease, which could indicate a subtle change in the diffusion mechanism at higher temperatures. This behavior has also been reported in the extraction of TPC from food by-products and brewer's grains (Alonso-Riaño et al., 2020; Patil et al., 2021). The Weibull model, with negative values of m and a decrease in b, suggested rapid extraction at the beginning and a subsequent slowdown, a pattern typical of systems where internal diffusion limits the process, as has been reported in the extraction of TPC from grape and jabuticaba by-products (Fernandes et al., 2020; Natolino & Da Porto, 2020). In the parabolic diffusion model, the initial extraction constant (A_0) increased from 1.065 to 1.620 as the temperature rose, suggesting greater availability of TPC at the beginning of the process due to higher thermal energy. Similarly, the diffusion constant (A_1) showed a general increase with temperature, indicating that the rate at which TPC diffuses through the plant matrix is higher at higher temperatures (Natolino & Da Porto, 2020). In Elovich's model, the constant E_0 increased proportionally with temperature, indicating that heat enhances the initial release of TPCs, possibly by facilitating the degradation of the plant matrix. On the other hand, the constant E_1, which describes the long-term rate, showed a slight increase, suggesting that although temperature accelerates the start of the process, the dynamics of subsequent extraction remain consistent, possibly limited by other factors such as internal diffusion or saturation (Natolino & Da Porto, 2020; Uvidia-Armijo, 2025). The comparison of experimental values and those predicted by mathematical models is shown in Figure 2.

Table 1. Mathematical models and regression constants in the extraction of total polyphenols from dried *I. guayusa* leaves with ultrasound assistance

Mathematical model		Constants in mathematical models				
		40 °C	50 °C	60 °C	70 °C	80 °C
Peleg model $C(t) = \frac{t}{k_1 + k_2 \cdot t}$	k_1	2.175	1.644	1.403	1.290	1.199
	k_2	0.297	0.294	0.286	0.273	0.256
Power law model $C(t) = B \cdot t^n$	B	0.987	1.130	1.263	1.305	1.440
	n	0.284	0.262	0.244	0.249	0.240
Weibull model $C(t) = C \cdot e^{-b \cdot t^m}$	C	94.340	94.954	47.247	73.210	77.207
	b	4.680	4.538	3.741	4.134	4.080
	m	-0.078	-0.073	-0.086	-0.077	-0.075
Parabolic Diffusion $C(t) = A_0 + A_1 \cdot \sqrt{t}$	A_0	1.065	1.251	1.420	1.460	1.620
	A_1	0.274	0.268	0.264	0.283	0.291
Elovich model $C(t) = E_0 + E_1 \cdot \ln(t)$	E_0	0.251	0.443	0.620	0.614	0.751
	E_1	0.700	0.689	0.680	0.724	0.741



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279 **Figure 2**. Experimental values of total polyphenols (g GAE/100 g) extracted from dried
280 leaves of *I. guayusa*, compared to values predicted by the Peleg (A), Power Law (B), Weibull
281 (C), parabolic diffusion (D) and Elovich (E) models.

The results presented in Table 2 show that most mathematical models accurately fit the experimental data on polyphenol extraction kinetics. To determine the suitability of each model, several statistical parameters were evaluated: coefficients of determination (R^2, adjusted R^2, and predicted R^2), root mean square deviation (RMSD), normalized root mean square deviation (NMRSD), and the Chi-square statistic (X^2).

R^2 indicates the proportion of the variance in the data explained by the model. In the Power law, Weibull, Parabolic Diffusion and Elovich models, the R^2 values ranged from 0.988 to 0.999, indicating that they can explain between 98 % and 99 % of the variability in the experimental values, which makes them reliable and representative models of the extraction phenomenon. In contrast, the Peleg model showed a lower fit with values between 0.876 and 0.947, indicating that it is the least suitable model for describing polyphenol extraction. To validate the predictive power of the models and avoid overfitting, the R^2-adjusted and R^2-predicted coefficients were compared. The R^2-adjusted compensates for the number of variables in the model, while the R-predicted evaluates the model's performance in making new predictions. Previous studies have indicated that a difference of less than 0.2 between these two values indicates a robust model without overfitting (Abreu-Naranjo et al., 2018; Che-Sulaiman et al., 2017; Pandey & Pandey, 2023). In this study, all the mathematical models analyzed meet this criterion at all temperatures, confirming their good predictive capacity and the absence of overfitting.

The RMSD and NMRSD values quantify the average error between experimental and predicted values, where low values indicate that the model has a small prediction error and, therefore, an accurate and desirable fit; conversely, high values reflect a larger error and a poor fit, which is undesirable in mathematical modelling (Karaoglu et al., 2025; Yogesha et al., 2020). In this regard, the Power law model stands out for its superiority, according to the RMSD and NMRSD values, which were less than 0.072 and 2.126 %, respectively. The X^2 value measures the overall discrepancy between the observed data and the data predicted by the model. Low values indicate that the model accurately reproduces the experimental data and is considered good, while high values suggest a poor fit and low explanatory power (Goual & Yousof, 2020; Zheng & Bentler, 2025). The Power law model presented the lowest values (<0.209 %), consolidating its position as the most suitable for describing the kinetics of polyphenol extraction.

Table 2. Statistical validation parameters of mathematical models for the extraction of total polyphenols from dried *I. guayusa* leaves with ultrasound assistance

Mathematical model		Statistical parameters				
		40 °C	50 °C	60 °C	70 °C	80 °C
Peleg model $C(t) = \frac{t}{k_1 + k_2 \cdot t}$	R^2	0.947	0.921	0.914	0.876	0.895
	R^2-Ajustado	0.930	0.890	0.880	0.848	0.865
	R^2-Predicho	0.924	0.884	0.874	0.838	0.852
	RMSD	0.133	0.155	0.158	0.186	0.185
	NMRSD (%)	4.257	4.729	4.660	5.125	4.771
	X^2 (%)	0.739	0.929	0.922	1201	1120
Power Law model $C(t) = B \cdot t^n$	R^2	0.989	0.997	0.997	0.999	0.989
	R^2-Ajustado	0.986	0.996	0.996	0.999	0.986
	R^2-Predicho	0.984	0.992	0.990	0.989	0.984
	RMSD	0.043	0.046	0.052	0.061	0.072
	NMRSD (%)	1.391	1.417	1.426	2.126	1.857
	X^2 (%)	0.079	0.084	0.099	0.209	0.171
Weibull model $C(t) = C \cdot e^{-b \cdot t^m}$	R^2	0.988	0.997	0.997	0.999	0.988
	R^2-Ajustado	0.985	0.996	0.996	0.999	0.985
	R^2-Predicho	0.984	0.986	0.980	0.966	0.976
	RMSD	0.044	0.063	0.072	0.099	0.088
	NMRSD (%)	1.403	1.915	2.110	2.726	2.254
	X^2 (%)	0.080	0.154	0.191	0.345	0.252
Parabolic Diffusion $C(t) = A_0 + A_1 \cdot \sqrt{t}$	R^2	0.986	0.991	0.989	0.996	0.986
	R^2-Ajustado	0.983	0.989	0.986	0.995	0.983
	R^2-Predicho	0.982	0.984	0.983	0.993	0.982
	RMSD	0.078	0.039	0.063	0.032	0.091
	NMRSD (%)	2.409	1.203	1.259	0.870	1.325
	X^2 (%)	0.234	0.060	0.067	0.035	0.086
Elovich model $C(t) = E_0 + E_1 \cdot \ln(t)$	R^2	0.982	0.994	0.995	0.994	0.984
	R^2-Ajustado	0.978	0.993	0.994	0.993	0.980
	R^2-Predicho	0.977	0.951	0.950	0.921	0.939
	RMSD	0.084	0.115	0.115	0.149	0.139
	NMRSD (%)	2.699	3.514	3.379	4.115	3.590
	X^2 (%)	0.300	0.521	0.492	0.789	0.648

R^2: coefficient of determination; RMSD: root mean square deviation; NMRSD: normalized root mean square deviation; X^2: chi-square

Thermodynamic parameters of activation

The Power Law model was selected as the best-fitting model based on its superior statistical performance (Table 2). To obtain the apparent rate constant (k) from this model, a reference time of 10 min was chosen, as it falls within the initial extraction phase where the extraction rate is highest and most sensitive to temperature changes. This time point was therefore considered the most suitable for determining the kinetic parameters of the process.

The Arrhenius model (Figure 3A) was used to determine the activation energy (E_a). Linear regression was performed by plotting the natural logarithm of the rate constant (ln k) against the inverse of the absolute temperature (1/T). The product of the slope of the line (-1057.042) and the universal gas constant gave the E_a. The coefficient of determination (R^2 = 0.928) indicated a good linear fit, validating the application of the model. On the other hand, Eyring's model (Figure 3B) was used to calculate the enthalpy (ΔH) and activation entropy (ΔS). In this case, linear regression was obtained by plotting the logarithm of the rate constant divided by temperature (ln(k/T)) as a function of the inverse of absolute temperature (1/T). The slope of the line (-204.991) is directly related to ΔH, while the intercept with the y-axis is associated with ΔS. The coefficient of determination (R^2=0.978) demonstrated good linearity of the model, confirming its suitability for determining these thermodynamic parameters. Both graphs with negative slopes are consistent with the nature of the extraction process, where an increase in temperature increases the reaction rate.

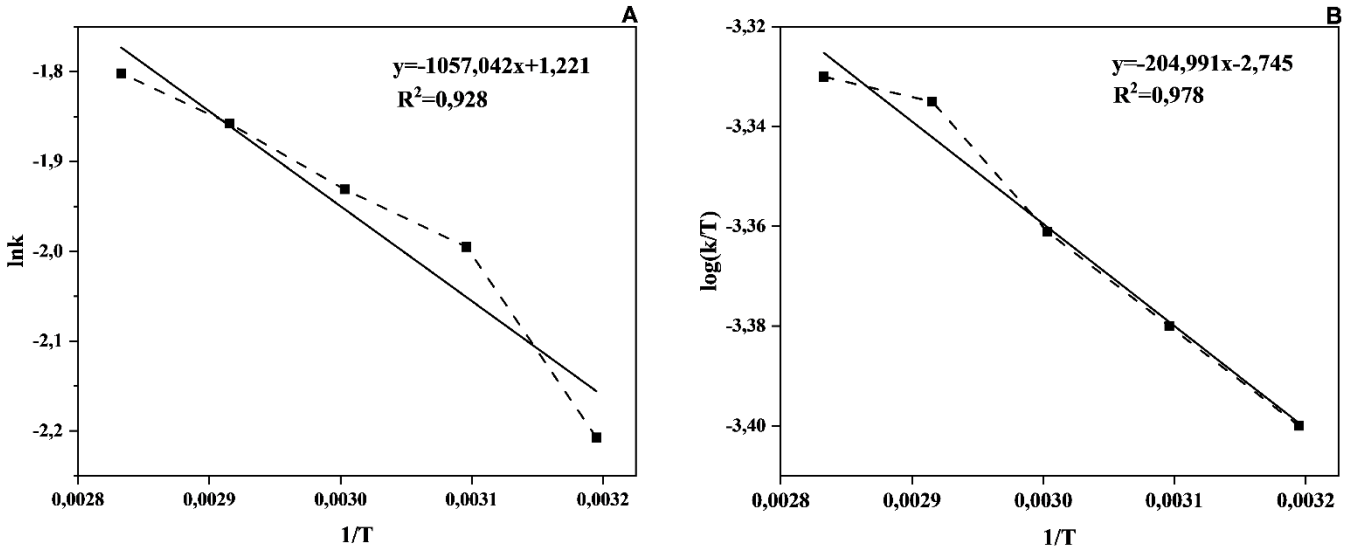

Figure 3. Determination of activation energy, enthalpy, and entropy of ultrasound-assisted extraction of total polyphenols from dried *I. guayusa* leaves. Linear regression using the Arrhenius model (A) and the Eyring model (B).

The E_a in ultrasound-assisted extraction of polyphenols represents the minimum energy barrier that molecules must overcome for the transfer of polyphenols from plant material to the solvent to occur. A low E_a value indicates that the process is facilitated by ultrasound, as cavitation and mechanical effects break down cell walls and promote the release of bioactive compounds (Dzah et al., 2020; Kumar & Bhaduri, 2025). In this study, E_a was 8.79 kJ/mol, confirming that the process is efficient and requires little energy to initiate extraction (Table 3). This result differs from the values reported in other plant species. For example, in *Pinus elliottii*, a value of 12.26 kJ/mol was reported (Zhang et al., 2024). In *Ananas comosus* residues, E_a was 48.23 kJ/mol (Kumar & Bhaduri, 2025). In *Malus domestica*, 7,14 kJ/mol was found (Hobbi et al., 2021). These differences can be attributed to the cellular structure, the type of polyphenols predominant in the plant material, the interaction with the solvent, and the mathematical model used (Borah et al., 2024; Lazar et al., 2016). On the other hand,

authors such as González-Centeno et al. (2015) and Wang et al. (2002) have pointed out that if E_a is less than 20 kJ/mol, the extraction process is mainly controlled by diffusion. On the other hand, if E_a exceeds 40 kJ/mol, the dominant mechanism is the solubilisation reaction. In this sense, the process of extracting polyphenols from *I. guayusa* leaves falls within the diffusion process.

In this study, the ΔH value (3.925 kJ/mol) obtained for polyphenol extraction indicates an endothermic process, i.e., one that requires heat absorption to facilitate the transfer of these compounds from the plant matrix to the solvent. Although this value is lower than those reported in the literature for other plant matrices, such as the 16.3 kJ/mol found in *Camellia sinensis* (green tea) leaves (Levan et al., 2024), and 14.44 kJ/mol in roots of *Ximenia americana* (Sidonie-Beatrice et al., 2018), remains consistent with the general trend that polyphenol extraction is favored by increased temperature. A low ΔH value may be due to a more accessible plant matrix, a more efficient solvent, or optimized experimental conditions, implying that less energy is required to break the interactions between polyphenols and the matrix (Sridhar et al., 2021). Furthermore, the literature indicates that extraction enthalpy is influenced by factors such as solvent type, solid-liquid ratio, particle size, and extraction method, and these parameters can reduce the energy required (Jurinjak-Tušek et al., 2016; Levan et al., 2024).

ΔS refers to the change in the degree of disorder or randomness of the system when the transition state is formed. A positive value of 145.03 J/molK suggests that the transition state is much more disordered than the initial state, which is characteristic of processes in which molecules pass from a more ordered state within the plant matrix to a more disordered state dissolved in the solvent (Gai et al., 2024). Furthermore, the literature indicates that ΔS is not only associated with disorder, but also with the ability of molecules to adopt different configurations and conformations, especially when methods such as ultrasound are used, which facilitate the breakdown of structures and the dispersion of extracted compounds (Bahloul et al., 2011; Alzeer, 2022).

ΔG is a critical thermodynamic parameter that determines the feasibility and spontaneity of the extraction process, as it describes the energy barrier that must be overcome for the reaction or mass transfer to occur (Fayaz et al., 2020). The value obtained of -47.271 kJ/mol for the extraction of polyphenols from *I. guayusa* indicates that the process is thermodynamically favorable and spontaneous, implying that the transition state is significantly more stable than the reactants in their initial state (Cao, 2025). The negative value reflects that the energy required to overcome the activation barrier is compensated by the stabilization of the transition state. The combination of ultrasound assistance and temperature not only accelerates the reaction kinetics but also energetically favors the formation of the transition state, allowing extraction to occur efficiently without the need for external energy input.

Table 3. Thermodynamic parameters of activation in the extraction of total polyphenols from dried *I. guayusa* leaves with ultrasound assistance

Parameter	Value
Activation energy (kJ/mol)	8.790 ± 1.211
Enthalpy (kJ/mol)	3.925 ± 1.157
Entropy (J/molK)	145.030 ± 3.122
Gibbs free energy at 80 °C (kJ/mol)	-47,271 ± 1.498

Conclusions

Ultrasound-assisted extraction of polyphenols from *Ilex guayusa* was shown to be an efficient process, directly influenced by extraction temperature and time. It was observed that increasing both parameters resulted in a higher concentration of total polyphenols. Five mathematical models were evaluated to describe the extraction behavior. The Power law model was identified as the most suitable for representing the kinetics of the experimental data, outperforming other models in terms of statistical fit. Analysis of the parameters of this model indicated that increasing the temperature improved the extraction rate. Although other models also showed a good fit to the experimental data, the Power law model stood out for its superiority, making it a robust predictive tool for optimizing the extraction process at an industrial level. The thermodynamic parameters revealed that extraction was an endothermic and spontaneous process, with low activation energy typical of diffusion-dominated systems. The positive entropy value indicated an increase in molecular disorder during extraction, favored by ultrasonic cavitation. These results underscore the advantage of ultrasound in reducing energy consumption compared to conventional methods.

Author contribution

SBLF: Writing – review & editing, investigation, data curation, conceptualization. EJCC: Review & editing. MR: Writing – review & editing, conceptualization. YGQ: Investigation, methodology. YAC: Methodology, data curation, investigation.

Declaration of competing interest

The authors have no competing interests to declare that are relevant to the contents of this article.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request

Referencias

Abishli, R., Albarri, R., & Şahin, S. (2021). Mass transfer, kinetics, and thermodynamics studies during the extraction of polyphenols from *Feijoa sellowiana* peels. *Journal of Food Processing and Preservation*, *45*(9), e15736. https://doi.org/10.1111/JFPP.15736

Abreu-Naranjo, R., Arteaga-Crespo, Y., Bravo-Sanchez, L., Pérez-Quintana, M., & García-Quintana, Y. (2018). Response surface methodology for optimisation of total polyphenol content and antioxidant activity of extracts from *Maytenus macrocarpa* bark by means of ultrasound-assisted extraction. *Wood Science and Technology*, *52*(5), 1359–1376. https://doi.org/10.1007/s00226-018-1034-x

Agu, C., & Agulanna, A. (2020). Kinetics and Thermodynamics of Oil Extracted from Amaranth. *Nutritional Value of Amaranth*. https://doi.org/10.5772/intechopen.88344

Alonso-Riaño, P., Diez, M. T. S., Blanco, B., Beltrán, S., Trigueros, E., & Benito-Román, O. (2020). Water Ultrasound-Assisted Extraction of Polyphenol Compounds from Brewer's Spent Grain: Kinetic Study, Extract Characterization, and Concentration. *Antioxidants*, *9*(3), 265. https://doi.org/10.3390/ANTIOX9030265

Altemimi, A., Watson, D. G., Choudhary, R., Dasari, M. R., & Lightfoot, D. A. (2016). Ultrasound Assisted Extraction of Phenolic Compounds from Peaches and Pumpkins. *PLOS ONE*, *11*(2), e0148758. https://doi.org/10.1371/JOURNAL.PONE.0148758

Alzeer, J. (2022). Directionality of Chemical Reaction and Spontaneity of Biological Process in the Context of Entropy. *International Journal of Regenerative Medicine*, 1–7. https://doi.org/10.31487/j.rgm.2022.02.06

Antony, A., & Farid, M. (2022). Effect of Temperatures on Polyphenols during Extraction. *Applied Sciences*, *12*(4), 2107. https://doi.org/10.3390/APP12042107

Arteaga-Crespo, Y., Radice, M., Bravo-Sanchez, L. R., García-Quintana, Y., & Scalvenzi, L. (2020). Optimisation of ultrasound-assisted extraction of phenolic antioxidants from *Ilex guayusa* Loes. leaves using response surface methodology. *Heliyon*, *6*(1), e03043. https://doi.org/10.1016/j.heliyon.2019.e03043

Bahloul, N., Boudhrioua, N., Kouhila, M., & Kechaou, N. (2011). Convective solar drying of olive leaves. *Journal of Food Process Engineering*, *34*(4), 1338–1362. https://doi.org/10.1111/J.1745-4530.2009.00432.X;PAGE:STRING:ARTICLE/CHAPTER

Borah, A., Gogoi, M., Goswami, R., & Hazarika, S. (2024). Ultrasound assisted hydrotropic extraction of polyphenols from green tea leaves in aqueous media. *Industrial Crops and Products*, *209*, 117986. https://doi.org/10.1016/J.INDCROP.2023.117986

Bucić-Kojić, A., Planinić, M., Tomas, S., Bilić, M., & Velić, D. (2007). Study of solid–liquid extraction kinetics of total polyphenols from grape seeds. *Journal of Food Engineering*, *81*(1), 236–242. https://doi.org/10.1016/J.JFOODENG.2006.10.027

Cadena-Carrera, S., Tramontin, D. P., Bella Cruz, A., Bella Cruz, R. C., Müller, J. M., & Hense, H. (2019). Biological activity of extracts from guayusa leaves (*Ilex guayusa* Loes.) obtained by supercritical CO2 and ethanol as cosolvent. *The Journal of Supercritical Fluids*, *152*, 104543. https://doi.org/10.1016/J.SUPFLU.2019.104543

Cadena-Carrera, S., Tramontin, D. P., Jacques, R., Scapin, E., Müller, J. M., & Hense, H. (2023). Green-based methods to obtain bioactive compounds from *Ilex guayusa* Loes. using polar solvent. *Natural Product Research*, *37*(18), 3103–3108. https://doi.org/10.1080/14786419.2022.2140802

Cao, G. J. (2025). Advancements in Machine Learning Predicting Activation and Gibbs Free Energies in Chemical Reactions. *International Journal of Quantum Chemistry*, *125*(7), e70036. https://doi.org/10.1002/QUA.70036;PAGEGROUP:STRING:PUBLICATION

Che Sulaiman, I. S., Basri, M., Fard Masoumi, H. R., Chee, W. J., Ashari, S. E., & Ismail, M. (2017). Effects of temperature, time, and solvent ratio on the extraction of phenolic compounds and the anti-radical activity of *Clinacanthus nutans* Lindau leaves by response surface methodology. *Chemistry Central Journal*, *11*(1), 1–11. https://doi.org/10.1186/S13065-017-0285-1/TABLES/6

Chianese, G., Golin-Pacheco, S. D., Taglialatela-Scafati, O., Collado, J. A., Munoz, E., Appendino, G., & Pollastro, F. (2019). Bioactive triterpenoids from the caffeine-rich plants guayusa and maté. *Food Research International*, *115*, 504–510. https://doi.org/10.1016/J.FOODRES.2018.10.005

Chóez-Guaranda, I., Viteri-Espinoza, R., Barragán-Lucas, A., Quijano-Avilés, M., & Manzano, P. (2022). Effect of solvent-solvent partition on antioxidant activity and GC-MS profile of *Ilex guayusa* Loes. leaves extract and fractions. *Natural Product Research*, *36*(6), 1570–1574. https://doi.org/10.1080/14786419.2021.1882455;SUBPAGE:STRING:ACCESS

Dzah, C. S., Duan, Y., Zhang, H., Wen, C., Zhang, J., Chen, G., & Ma, H. (2020). The effects of ultrasound assisted extraction on yield, antioxidant, anticancer and antimicrobial activity of polyphenol extracts: A review. *Food Bioscience*, *35*, 100547. https://doi.org/10.1016/J.FBIO.2020.100547

Espinoza-Vasquez, A. P., Angulo, W., De Cecchis, D., Gonzalez, Y., Galatro, D., Manzano, P., & Choez-Guaranda, I. (2023). Mathematical Modeling of the Kinetics of Released Antioxidant Compounds During Solid-Liquid Extraction for a Nutraceutical Beverage from *Ilex Guayusa*, Vernonanthura Patens, and Cocoa Husk Plants. *Chemical Engineering Transactions*, *102*(May), 289–294. https://doi.org/10.3303/CET23102049

Fayaz, A., Siskos, M. G., Varras, P. C., Choudhary, M. I., Atia-Tul-Wahab, & Ioannis, G. P. (2020). The unique catalytic role of water in aromatic C-H activation at neutral pH: A combined NMR and DFT study of polyphenolic compounds. *Physical Chemistry Chemical Physics*, *22*(30), 17401–17411. https://doi.org/10.1039/d0cp02826f

Fernandes, F. A. N., Fonteles, T. V., Rodrigues, S., de Brito, E. S., & Tiwari, B. K. (2020). Ultrasound-assisted extraction of anthocyanins and phenolics from jabuticaba

(*Myrciaria cauliflora*) peel: kinetics and mathematical modeling. *Journal of Food Science and Technology*, *57*(6), 2321–2328. https://doi.org/10.1007/S13197-020-04270-3/METRICS

Gai, Z. Y., Wang, Y., Xian, M. H., Tang, D., & Wang, S. M. (2024). Comprehensive assessment of the extraction of *Phyllanthus emblica* L. based on the G1-Entropy Method and Response Surface Methodology. *Journal of Applied Research on Medicinal and Aromatic Plants*, *39*, 100536. https://doi.org/10.1016/J.JARMAP.2024.100536

García-Ruiz, A., Baenas, N., Benítez-González, A. M., Stinco, C. M., Meléndez-Martínez, A. J., Moreno, D. A., & Ruales, J. (2017). Guayusa (*Ilex guayusa* L.) new tea: phenolic and carotenoid composition and antioxidant capacity. *Journal of the Science of Food and Agriculture*, *97*(12), 3929–3936. https://doi.org/10.1002/JSFA.8255

Gomez-Molina, M., Albaladejo-Marico, L., Yepes-Molina, L., Nicolas-Espinosa, J., Navarro-León, E., Garcia-Ibañez, P., & Carvajal, M. (2024). Exploring Phenolic Compounds in Crop By-Products for Cosmetic Efficacy. *International Journal of Molecular Sciences*, *25*(11). https://doi.org/10.3390/ijms25115884

González-Centeno, M. R., Comas-Serra, F., Femenia, A., Rosselló, C., & Simal, S. (2015). Effect of power ultrasound application on aqueous extraction of phenolic compounds and antioxidant capacity from grape pomace (*Vitis vinifera* L.): Experimental kinetics and modeling. *Ultrasonics Sonochemistry*, *22*, 506–514. https://doi.org/10.1016/J.ULTSONCH.2014.05.027

Gorji, R., Skvaril, J., & Odlare, M. (2024). Determining Moisture Content of Basil Using Handheld Near-Infrared Spectroscopy. *Horticulturae*, *10*(4). https://doi.org/10.3390/horticulturae10040336

Goual, H., & Yousof, H. M. (2020). Validation of Burr XII inverse Rayleigh model via a modified chi-squared goodness-of-fit test. *Journal of Applied Statistics*, *47*(3), 393–423. https://doi.org/10.1080/02664763.2019.1639642

Haslina, H., Larasati, D., Pratiwi, E., Nazir, N., & Fitriana, I. (2021). Optimization of temperature and extraction time for the nutritional and phytochemical contents of corn bran with ultrasonic-method. *AJARCDE*, *5*(3), 32–42. https://doi.org/10.29165/AJARCDE.V5I3.77

Hobbi, P., Okoro, O. V., Delporte, C., Alimoradi, H., Podstawczyk, D., Nie, L., Bernaerts, K. V., & Shavandi, A. (2021). Kinetic modelling of the solid–liquid extraction process of polyphenolic compounds from apple pomace: influence of solvent composition and temperature. *Bioresources and Bioprocessing*, *8*(1). https://doi.org/10.1186/s40643-021-00465-4

Huang, H., Cui, P., Lu, G., Wang, X., Jiang, L., & Luo, Y. (2023). Photosynthetic and Antioxidant Responses of *Gymnocarpos przewalskii* to Simulated Rainfall Changes. *Forests*, *14*(4), 789. https://doi.org/10.3390/F14040789

John, S. U., Igbokwe, P. K., Nwabanne, J. T., Onu, C. E., Nweke, C. N., & Ejiofor, C. C. (2024). Development of Second-Generation Feedstock Towards Environmental Sustainability: Biobased Oil Extraction, Thermodynamics and Advanced Nonlinear

Kinetic Modeling. *Green Energy and Environmental Technology*, *3*. https://doi.org/10.5772/GEET.20240046

Jurinjak-Tušek, A., Benković, M., Belščak Cvitanović, A., Valinger, D., Jurina, T., & Gajdoš Kljusurić, J. (2016). Kinetics and thermodynamics of the solid-liquid extraction process of total polyphenols, antioxidants and extraction yield from Asteraceae plants. *Industrial Crops and Products*, *91*, 205–214. https://doi.org/10.1016/J.INDCROP.2016.07.015

Kabudi, N., Shayanfar, A., Acree, W. E., & Jouyban, A. (2022). Correlation of Surface Tension of Mono-Solvents at Various Temperatures. *Liquids*, *2*(4), 378–387. https://doi.org/10.3390/LIQUIDS2040021

Kaltsa, O., Lakka, A., Grigorakis, S., Karageorgou, I., Batra, G., Bozinou, E., Lalas, S., & Makris, D. P. (2020). A Green Extraction Process for Polyphenols from Elderberry (*Sambucus nigra*) Flowers Using Deep Eutectic Solvent and Ultrasound-Assisted Pretreatment. *Molecules*, *25*(4), 921. https://doi.org/10.3390/MOLECULES25040921

Karaoglu, S., Imran, M., & McKinney, B. A. (2025). Network-based SEITR epidemiological model with contact heterogeneity: comparison with homogeneous models for random, scale-free and small-world networks. *The European Physical Journal Plus*, *140*(6), 1–29. https://doi.org/10.1140/EPJP/S13360-025-06481-Z

Kelebek, H., Sasmaz, H. K., Aksay, O., Selli, S., Kahraman, O., & Fields, C. (2024). Exploring the Impact of Infusion Parameters and In Vitro Digestion on the Phenolic Profile and Antioxidant Capacity of Guayusa (*Ilex guayusa* Loes.) Tea Using Liquid Chromatography, Diode Array Detection, and Electrospray Ionization Tandem Mass Spectrometr. *Foods*, *13*(5). https://doi.org/10.3390/foods13050694

Kinetik, K., Fenolik Daripada Ekstrak, J. K., Piper, D., Menggunakan, L., Subkritikal, A., Nur,), Rahmah, L., Mazlina, S., Kamal, M., Sulaiman, A., Saleena Taip, F., Shamsul, &, & Siajam, I. (2023). Kinetic Study of Total Phenolic Content from *Piper betle* Linn. Leaves Extract Using Subcritical Water. *Sains Malaysiana*, *52*(6), 1737–1747. https://doi.org/10.17576/jsm-2023-5206-10

Kobus, Z., Krzywicka, M., Pecyna, A., & Buczaj, A. (2021). Process Efficiency and Energy Consumption during the Ultrasound-Assisted Extraction of Bioactive Substances from Hawthorn Berries. *Energies*, *14*(22), 7638. https://doi.org/10.3390/EN14227638

Kumar, R., & Bhaduri, G. A. (2025). Biorefining of pine cone forest waste: Ultrasound assisted extraction followed with thermal degradation for a zero waste process. *Industrial Crops and Products*, *224*, 120278. https://doi.org/10.1016/J.INDCROP.2024.120278

Lazar, L., Talmaciu, A. I., Volf, I., & Popa, V. I. (2016). Kinetic modeling of the ultrasound-assisted extraction of polyphenols from *Picea abies* bark. *Ultrasonics Sonochemistry*, *32*, 191–197. https://doi.org/10.1016/J.ULTSONCH.2016.03.009

Levan, G., Tamar, K., & Tamar, T. (2024). Modeling of polyphenols extraction process from green tea and the effect of temperature on the process. *International Journal of Science and Research Archive*, *12*(1), 2115–2124.

https://doi.org/10.30574/ijsra.2024.12.1.0983

Liu, H., Liu, D., Wang, W., Zhang, X., Tuly, J., Li, H., & Ma, H. (2024). Dual-frequency countercurrent ultrasonic-assisted extraction of the cold brew coffee and in situ real-time monitoring of extraction process. *Ultrasonics Sonochemistry*, *111*, 107118. https://doi.org/10.1016/J.ULTSONCH.2024.107118

Liu, W., Cui, X., Zhong, Y., Ma, R., Liu, B., & Xia, Y. (2023). Phenolic metabolites as therapeutic in inflammation and neoplasms: Molecular pathways explaining their efficacy. *Pharmacological Research*, *193*, 106812. https://doi.org/10.1016/J.PHRS.2023.106812

Liu, Y., Zhe, W., Zhang, R., Peng, Z., Wang, Y., Gao, H., Guo, Z., & Xiao, J. (2022). Ultrasonic-assisted extraction of polyphenolic compounds from Paederia scandens (Lour.) Merr. Using deep eutectic solvent: optimization, identification, and comparison with traditional methods. *Ultrasonics Sonochemistry*, *86*, 106005. https://doi.org/10.1016/J.ULTSONCH.2022.106005

Mahfud, M., Nabila, A. R., & Variyana, Y. (2025). Developing a kinetic model for microwave hydro diffusion and gravity with steam flow on extraction of essential oils from *Amomum compactum* seeds. *Rasayan Journal of Chemistry*, *18*(1), 52–60. https://doi.org/10.31788/RJC.2025.1819024

Marhamati, M., Kheirati Kakhaki, Z., & Rezaei, M. (2020). Advance in Ultrasound-Assisted Extraction of Edible Oils: A Review. *Journal of Nutrition,Fasting and Health*, *8*(4), 220–230. https://doi.org/10.22038/JNFH.2020.51138.1288

Mattos, R., & Zecchi, B. (2025). Modeling, simulation, and optimization of multi-stage equilibrium extraction of phenolic compounds from grape pomace. *Journal of Food Engineering*, *389*, 112392. https://doi.org/10.1016/J.JFOODENG.2024.112392

Meneses, M. Á., Guzmán, J., Cabrera, J., Magallanes, J., Valarezo, E., & Guamán-Balcázar, M. del C. (2024). Green Processing of *Ilex guayusa*: Antioxidant Concentration and Caffeine Reduction Using Encapsulation by Supercritical Antisolvent Process. *Molecules*, *29*(22), 5309. https://doi.org/10.3390/MOLECULES29225309

Mwamatope, B., Tembo, D., Kampira, E., Maliwichi-Nyirenda, C., & Ndolo, V. (2021). Seasonal Variation of Phytochemicals in Four Selected Medicinal Plants. *Pharmacognosy Research*, *13*(4), 218–226. https://doi.org/10.5530/pres.13.4.14

Natolino, A., & Da Porto, C. (2020). Kinetic models for conventional and ultrasound assistant extraction of polyphenols from defatted fresh and distilled grape marc and its main components skins and seeds. *Chemical Engineering Research and Design*, *156*, 1–12. https://doi.org/10.1016/J.CHERD.2020.01.009

Pandey, B. K., & Pandey, D. (2023). Parametric optimization and prediction of enhanced thermoelectric performance in co-doped CaMnO3 using response surface methodology and neural network. *Journal of Materials Science: Materials in Electronics*, *34*(21), 1–24. https://doi.org/10.1007/S10854-023-10954-1/METRICS

Patil, S. S., Deshannavar, U. B., Ramasamy, M., Emani, S., Khalilpoor, N., & Issakhov, A.

(2021). Study of Extraction Kinetics of Total Polyphenols from Curry Leaves. *International Journal of Chemical Engineering*, *2021*(1), 9988684. https://doi.org/10.1155/2021/9988684

Rebollo-Hernanz, M., Cañas, S., Taladrid, D., Segovia, Á., Bartolomé, B., Aguilera, Y., & Martín-Cabrejas, M. A. (2021). Extraction of phenolic compounds from cocoa shell: Modeling using response surface methodology and artificial neural networks. *Separation and Purification Technology*, *270*, 118779. https://doi.org/10.1016/J.SEPPUR.2021.118779

Rodríguez-Pérez, C., Segura-Carretero, A., & del Mar Contreras, M. (2019). Phenolic compounds as natural and multifunctional anti-obesity agents: A review. *Critical Reviews in Food Science and Nutrition*, *59*(8), 1212–1229. https://doi.org/10.1080/10408398.2017.1399859

Rusu, M., Ghendov-Mosanu, A., Sturza, R., Rusu, M., Ghendov-Mosanu, A., & Sturza, R. (2021). Application of Polynomial Mathematical Models for the Extraction of Bioactive Compounds from Plant Sources. *Applied Mathematics*, *12*(11), 1126–1144. https://doi.org/10.4236/AM.2021.1211072

Sidonie-Beatrice, K., Benoit, N. M., Tsague, T., Karole, R., Djiobie, T., Eléonore, G., Jean, M., & Alain, K. (2018). Kinetics and Thermodynamics of Total Polyphenolic Compounds Microwave Assisted Extraction from the Roots of Ximeniaamericana (Olacaceae). *International Journal of Science and Research*. https://doi.org/10.21275/SR20525214232

Silva-Paz, R. J., Mateo-Mendoza, D. K., & Eccoña-Sota, A. (2023). Mathematical Modelling of Muña Leaf Drying (*Minthostachys mollis*) for Determination of the Diffusion Coefficient, Enthalpy, and Gibbs Free Energy. *ChemEngineering*, *7*(3), 49. https://doi.org/10.3390/CHEMENGINEERING7030049

Sridhar, A., Ponnuchamy, M., Kumar, P. S., Kapoor, A., Vo, D. V. N., & Prabhakar, S. (2021). Techniques and modeling of polyphenol extraction from food: a review. *Environmental Chemistry Letters*, *19*(4), 3409–3443. https://doi.org/10.1007/S10311-021-01217-8

Sun, S., Liu, Z., Lin, M., Gao, N., & Wang, X. (2024). Polyphenols in health and food processing: antibacterial, anti-inflammatory, and antioxidant insights. *Frontiers in Nutrition*, *11*, 1456730. https://doi.org/10.3389/FNUT.2024.1456730/BIBTEX

Teoh, Y. P., Othman, N., Sam, S. T., Ooi, Z. X., Liu, W. W., Walli, S., Tan, L. S., & Lee, B. B. (2024). Extraction of Bioactive Secondary Metabolites from *Citrus Maxima* Peel Via Pressurized Hot Water Extractor for the Synthesis of Iron Oxide Nanoparticles. *International Journal of Nanoelectronics and Materials*, *17*(Special Issue), 119–131. https://doi.org/10.58915/ijneam.v17iJune.845

Uvidia Armijo, L. A. (2025). Mathematical modeling of the extraction of bioactive compounds present in the leaves of *Annona muricata* L. *African Journal of Biomedical Research*, *28*(January), 598–603. https://doi.org/10.53555/ajbr.v28i1s.6173

Villacís-Chiriboga, J., García-Ruiz, A., Baenas, N., Moreno, D. A., Meléndez-Martínez, A.

J., Stinco, C. M., Jerves-Andrade, L., León-Tamariz, F., Ortiz-Ulloa, J., & Ruales, J. (2018). Changes in phytochemical composition, bioactivity and in vitro digestibility of guayusa leaves (*Ilex guayusa* Loes.) in different ripening stages. *Journal of the Science of Food and Agriculture*, *98*(5), 1927–1934. https://doi.org/10.1002/JSFA.8675;REQUESTEDJOURNAL:JOURNAL:10970010;WGROUP:STRING:PUBLICATION

Villamil-Galindo, E., & Piagentini, A. M. (2024). Kinetic modeling of valuable phenolic compounds extraction from strawberry and apple agro-industrial by-products. *Journal of Food Process Engineering*, *47*(3), e14573. https://doi.org/10.1111/JFPE.14573

Wang, P., Cheng, C., Ma, Y., & Jia, M. (2020). Degradation behavior of polyphenols in model aqueous extraction system based on mechanical and sonochemical effects induced by ultrasound. *Separation and Purification Technology*, *247*, 116967. https://doi.org/10.1016/J.SEPPUR.2020.116967

Wang, Y. G., Yue, S. T., Li, D. Q., Jin, M. J., & Li, C. Z. (2002). Kinetics and mechanism of Y(III) extraction with CA-100 using a constant interfacial cell with laminar flow. *Solvent Extraction and Ion Exchange*, *20*(3), 345–358. https://doi.org/10.1081/SEI-120004809;SUBPAGE:STRING:ABSTRACT;JOURNAL:JOURNAL:LSEI20;WGROUP:STRING:PUBLICATION

Yogesha, M., Rao, V. G., Devangad, P., D'Souza, J. S., & Chidangil, S. (2020). A chemometric study combined with spectroscopy for the quantification of secondary structure of flagellar-associated protein 174 (FAP174). *Journal of Chemometrics*, *34*(5), 1–14. https://doi.org/10.1002/cem.3221

Yusoff, I. M., Mat Taher, Z., Rahmat, Z., & Chua, L. S. (2022). A review of ultrasound-assisted extraction for plant bioactive compounds: Phenolics, flavonoids, thymols, saponins and proteins. *Food Research International*, *157*, 111268. https://doi.org/10.1016/J.FOODRES.2022.111268

Zhang, S., Xie, H., Huang, J., Chen, Q., Li, X., Chen, X., Liang, J., & Wang, L. (2024). Ultrasound-assisted extraction of polyphenols from pine needles (*Pinus elliottii*): Comprehensive insights from RSM optimization, antioxidant activity, UHPLC-Q-Exactive Orbitrap MS/MS analysis and kinetic model. *Ultrasonics Sonochemistry*, *102*, 106742. https://doi.org/10.1016/J.ULTSONCH.2023.106742

Zheng, B. Q., & Bentler, P. M. (2025). Enhancing Model Fit Evaluation in SEM: Practical Tips for Optimizing Chi-Square Tests. *Structural Equation Modeling*, *32*(1), 136–141. https://doi.org/10.1080/10705511.2024.2354802;PAGE:STRING:ARTICLE/CHAPTER

Zhu, X., Das, R. S., Bhavya, M. L., Garcia-Vaquero, M., & Tiwari, B. K. (2024). Acoustic cavitation for agri-food applications: Mechanism of action, design of new systems, challenges and strategies for scale-up. *Ultrasonics Sonochemistry*, *105*, 106850. https://doi.org/10.1016/J.ULTSONCH.2024.106850