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Research article

Extraction of bioactive compounds from yerba mate (*Ilex paraguariensis St.-Hil.*) leaves by packed-bed extractor using hot water as solvents: Kinetics study and mathematical modeling

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Abstract: The aqueous packed-bed extraction of bioactive compounds from yerba mate leaves was evaluated given their potential application in the food industry. The influence of temperature (50–70 °C) and feed flow rate (10–20 cm^3/min) was investigated by central composite design. A mathematical model derived from the differential equation of mass conservation in solid and liquid phases was used to describe the concentration of total phenolic concentration over time, considering a finite volume-based algorithm to solve this multiscale model along the column length and particle radius. The findings demonstrated that higher temperatures improved bioactive chemical extraction yields, although feed flow rate played a role at low temperatures because it improved external mass transfer. Caffeic acid, caffeine, and chlorogenic acid were the principal bioactive chemicals studied, with the highest concentrations extracted being 156.3×10^{-2}, 273.5×10^{-2}, and 351.6×10^{-2} mg/g_{YM} (mg of bioactive per g of yerba mate), respectively, obtained after 60 minutes of extraction process at 70 °C and a flow rate of 10 cm^3/min. The amount of these predominant bioactive compounds extracted exceeded 90% of the total content that could be obtained using water as a solvent. The mathematical model evaluated showed relative mean errors lower than 3% and R^2 higher than 98%, suggesting a

good fit for the experimental data, with the external mass transfer and effective intraparticle diffusion coefficients ranging between 8.75×10^{-8} to 1.77×10^{-6} m/s and 9.34×10^{-11} to 3.06×10^{-9} m²/s, respectively.

Keywords: green extraction process; fixed-bed extractor; caffeic acid; caffeine; diffusion coefficient

1. Introduction

Plants are currently being studied for their medical effects and chemical composition, with a focus on bioactive substances and antioxidant activity. Because of their efficiency, low cost, and lack of toxicity, the use of phytochemicals in the food business has drawn public and scientific interest. In addition, epidemiological and clinical evidence links diets rich in antioxidants with a reduced risk of degenerative diseases and reduced mortality [1]. In this context, yerba mate (*Ilex paraguariensis St.-Hil*.) showed a promising source of bioactive compounds, being. Yerba mate is predominantly cultivated in South America, notably in Brazil, Argentina, Paraguay, and Uruguay [2]. Approximately 500,000 tons of yerba mate were produced in Brazil in 2021, and the state of Paraná reached almost 37% of Brazilian production, highlighting its cultural and economic importance as an agro-industrial product [3]. Its consumption usually occurs in mate tea and tererê (iced tea), but there is growing interest in developing new products from this raw material.

In recent years, the interest of researchers in the properties of the biochemical components present in yerba mate has increased, especially the bioactive compounds, which promote benefits to human health. The literature suggests that the consumption of yerba mate provides dietary antioxidants that protect against the effects of free radicals [4]. In addition, mate tea has been reported to be anti-inflammatory, hypocholesterolemic, hepatoprotective, cardioprotective, central nervous system stimulant, and diuretic [5–8]. Studies indicate a high content of phytochemicals present in yerba mate (about 10% in dry weight), with emphasis on phenolic compounds, such as chlorogenic and caffeic acids; methylxanthine (caffeine and theobromine) and flavonoids (quercetin and rutin) [4,9,10].

It is vital to investigate the extraction method to obtain these bioactive chemicals from a solid matrix. Solvent extraction has been widely utilized for leaves due to its simplicity (no complex equipment required), good selectivity, and versatility with regulated recovery. The efficiency of the extraction process depends on several parameters such as temperature, time, particle size, solvent polarity, pH, and others [7]. Aqueous extraction is preferred over alcohols or organic solvents because it does not limit future applications in the food and pharmaceutical industries and does not generate harmful waste [11]. Many works report the solid-liquid extraction of bioactive compounds from yerba mate leaves by conventional solid-liquid extraction processes, such as maceration, infusion, batch extraction, hydro distillation, and Soxhlet extraction [12–14], or new techniques such as ultrasound-assistance extraction and supercritical fluids [15,16]. The major disadvantages of conventional techniques include low selectivity in concentration, the use of expensive high-purity solvents, and processes that take a long time for the contact between solid and the solvent to reach a balance [16], while these new extraction technologies (e.g., microwave-assisted extraction, supercritical fluid extraction, subcritical water extraction, and infrared-assisted extraction) require complex equipment/systems that limit their commercial application in the food industry [17].

The packed-bed extraction process is an alternative for obtaining valuable bioactive compounds from plant matrices. It is characterized by the continuous elution of a solvent via a fixed bed of solids included in a cylindrical container. Fresh solvent is constantly injected into the bed and moves through it at a constant rate, facilitating leaching across the bed. This technology, like supercritical fluid systems or pressurized liquid extractors, can utilize normal solvents (water or organic solvents) at low pressure and temperature adjustment. Due to the constant fresh solvent eluting the solid-packed bed, this system's solid/fluid contact time is usually much shorter than in high-efficiency batch operations. However, some phenomenological restrictions, such as internal and external mass transfer resistances, may be significant and must be evaluated [18,19].

Mathematical models are useful engineering tools that considerably simplify simulation, optimization, and design while contributing to lower energy, raw material, solvent costs, and process time. Yet, mathematical analysis makes it possible to estimate the mass transfer resistance and predict the adequate operational condition and design units for the industrial scale [11,20]. In this context, we aimed to evaluate the influence of the process variables (temperature and feed flow) in the extraction of bioactive compounds from yerba mate leaves by a packed-bed extraction process using hot water as a solvent. Additionally, a mathematical method was used to describe the solid-liquid extraction of bioactive compounds involved in the process.

2. Materials and methods

2.1. Materials and chemicals

Yerba mate leaves were obtained from Baldo S.A. (São Mateus do Sul, Paraná State, Brazil). The sample was processed using a multiprocessor and particle size distribution was performed using a set of Tyler series sieves (48 mesh). Acetonitrile (chromatography grade) was purchased from Honeywell (NC, USA). The standards of chlorogenic acid (5-caffeoylquinic acid), caffeic acid, caffeine, theobromine, rutin, and quercetin were purchased from Sigma–Aldrich Co. (São Paulo, São Paulo State, Brazil). All other chemicals used were of analytical grade.

2.2. Packed-bed extraction

Experiments were carried out in a bench-packed-bed extractor, adapted from Canteli et al. [21]. Deionized water was used as the solvent for the extraction process. A schematic representation of the process is depicted in Figure 1. The cylindrical jacketed column was filled with approximately 8 g of yerba mate (internal diameter of 8 mm and total height of 18 cm) and completed by glass sphere (diameter of 0.003 m) and glass wool on both ends to avoid clogging the extraction system. The temperature of the packed bed and feed flow solvent was kept constant using a thermostatic bath (Quimis, model Q215S). Packed-bed extraction experiments were performed for 60 minutes at different temperatures (50–70 °C) and flow rates (10–20 cm^3/min), following a randomized 2^2 experimental design with a central point, to assess process variable influence on the extraction of the bioactive compounds.

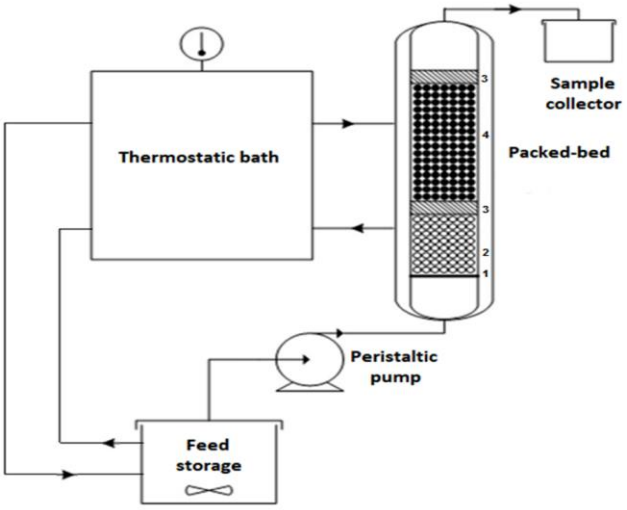

Figure 1. Schematic diagram of the packed-bed setup. (1) Column support; (2) glass spheres; (3) glass wool; and (4) yerba mate.

The bed porosity (ε) was estimated according to the methodology described by Rodrigues et al. [22]. The apparent density (ρ_{PB}) was calculated considering the amount of raw material needed to fill the total volume of the extraction vessel, according to Eq (1).

$$\rho_{PB} = \frac{M_{YM}}{V_{COLUMN}}, \tag{1}$$

where M_{YM} is the mass of the yerba mate sample loaded (g) and V_{COLUMN} is the column volume filled with yerba mate in the extraction vessel (cm³). The true density of yerba mate leaves (ρ_{YM}) was measured using a helium pycnometer at the Institute of Chemistry/UNICAMP, Campinas, Brazil. The packed-bed porosity was determined by the apparent (ρ_{PB}) and yerba mate real densities (ρ_{YM}) ratio, as Eq (2):

$$\varepsilon = 1 - \frac{\rho_{PB}}{\rho_{YM}}. \tag{2}$$

As a reference extraction procedure, the sequential batch extraction process was adapted from Panzl et al. [4], using deionized water as a solvent at 70 °C. This method evaluated the maximum quantity of bioactive compounds that could be extracted with water. Sachets containing 8 g of yerba mate were inserted into the jacketed tank with a propeller stirrer and fed 1000 g of water. The sachets were submerged and secured to avoid contact with the stirring propeller. A thermostatic heating bath (Quimis, Brazil) was used for the experiments. A thermometer was used to monitor the temperature with a propeller agitator (IKA, RW 20 digital) at 200 rpm. The yerba mate sachet underwent three batch extraction cycles: In each cycle, the sample was added to 1000 g of deionized water; after 1 h the liquid extract was removed, and 1000 g of deionized water was added again. The total extraction time was three hours using 3000 g of deionized water for 8 g of yerba mate.

2.3. Quantification of bioactive compounds

The total phenolic concentration (TPC) of the aqueous extract of yerba mate obtained from packed-bed extraction along the time operation was calculated by the Folin-Ciocalteau method [23]. All the tests were performed in triplicate and the results were expressed as milligrams of gallic acid equivalent (GAE) per gram of yerba mate (mg_{GAE}/g_{YM}).

To estimate the concentration of the most representative bioactive compounds obtained during the packed-bed extraction process, these extracts were analyzed by HPLC-DAD (Agilent 1260 series) equipped with a quaternary pump (G1311B), autosampler (G1329B), column compartment (G1316A) and a diode array detector (G4212B), associated with a ChemStation software (Rev B.04.03-SP1). The HPLC-DAD column was Zorbax Eclipse XDB-C18 (4.6 × 150 mm, 5 μm). The mobile phases were ultrapure water + 0.1% phosphoric acid (phase A) + acetonitrile (phase B) at a flow ratio of 0.8 cm^3/min. The gradient mode was: From 0 to 5 min with 4% of mobile phase B; from 5 to 10 min with 4% of B; from 10 to 20 min with 10% of B; from 20 to 30 min with 10% of B; 30 min with 20% of B until the end with 20% of phase B. The injection volume was 10 μL at the temperature of 33 °C. Calibration curves were prepared in the concentration range from 0.25 to 10 μg/L and using theobromine (273 nm), caffeine (273 nm), chlorogenic acid (322 nm), caffeic acid (325 nm), rutin (360 nm), and quercetin (258 and 380 nm) as standards for the compounds quantification. The results were expressed in milligrams of bioactive compound per gram of yerba mate (mg/g_{YM}).

2.4. Mathematical model and experimental setup

The mathematical model employed in this study is based on a multiscale approach aimed at describing mass transfer within the packed bed. A set of differential equations is utilized to ascertain the concentration within the solid particles at various positions (height) in the column, while a separate differential equation is applied to calculate the concentration in the liquid phase in contact with the particles. Consequently, this approach enables the determination of both the concentration along the particle's radius and throughout the column height as a function of the extraction time. This mathematical approach was previously applied in other studies, such as the supercritical fluids [24] and fixed-bed systems [19]. The solid matrix is assumed to be a pseudo-homogeneous medium and the evaluated bioactive compounds were considered single species. The solvent was fed through the bottom of the column flowed through the column and became richer in the bioactive compounds. Consequently, the concentration of bioactive compounds in the liquid phase, interacting with solid particles, varies with both time and position along the bed length. This information must be considered in the formulation of the mass conservation equation in the solid phase. The equations, respective boundaries, and initial conditions for each phase are presented below.

2.4.1. Mass balance applied in the solid phase

The hypotheses adopted in the formulation of the mass conservation equation for the solid phase are: (1) Particles are assumed to be a pseudo-homogeneous medium with constant physical properties; (2) the particles are assumed to be spheres with constant diameter; (3) no equilibrium relation is used to relate the bioactive compounds phase inside the solid with the concentration in the porous matrix, instead, mass balance is performed considering the total amount of bioactive compounds that can be

removed through exhaustive extraction using a sequential batch extraction process; (4) one-dimensional mass transfer in the radial direction of the solid matrix.

Based on the hypotheses, the bioactive compounds concentration in the solid phase (*Cs*) can be calculated from the following parabolic PDE in spherical coordinates Eq (3):

$$\frac{\partial Cs}{\partial t} = \frac{D_{EF}}{r} \times \frac{\partial}{\partial r}\left(r^2 \times \frac{\partial Cs}{\partial r}\right), \tag{3}$$

where: t is the time, D_{EF} is the effective diffusion coefficient of bioactive compounds, and r is the radial direction of the mass transfer flux. The boundary conditions at the center and external surface are described by Eqs (4) and (5), respectively:

$$\frac{\partial Cs}{\partial r} = 0, \text{ at r = 0}, \tag{4}$$

$$-D_{EF} \times \frac{\partial Cs}{\partial r} = K_F \times (C_S - C_F), \tag{5}$$

where: k_F is the external mass transfer coefficient, R is the particle radius, and CF is the bioactive compound concentration in the liquid phase. Since the concentration of bioactive compounds in the solid phase changes in the z-direction, the concentration C_S is a multiscale problem: $C_S = f(z,r,t)$.

For the initial condition, it is assumed the concentration of bioactive compounds inside the solid is constant and equal to the total amount of bioactive compounds removed in the exhaustive extraction divided by the mass of the solid used in packed-bed length ($C_{S,0}$). The concentration within the solid remains constant until the particle reaches the water, and this timing depends on the axial position within the packed bed relative to the superficial velocity (v_S). The initial condition can be expressed as Eq (6):

$$C_S = C_{S,0}, \text{ at } t < \frac{z}{v_S}, \tag{6}$$

2.4.2. Mass balance applied in the liquid phase

The hypotheses adopted in the formulation of the mass conservation equation for the liquid phase are (1) no radial dispersion; (2) constant porosity along the packed bed; (3) constant superficial velocity along the packed bed; and (4) bioactive compound concentration in the liquid phase changes only in the z-direction. Based on these hypotheses, the mass conservation for bioactive compounds concentration in the liquid phase (C_F) can be calculated by Eq (7):

$$\frac{\partial C_F}{\partial t} + V_S \times \frac{\partial C_F}{\partial z} = \frac{\partial}{\partial z}\left(D_L \times \frac{\partial C_F}{\partial z}\right) + \frac{1-\varepsilon}{\varepsilon} \times \frac{3}{R} \times K_F \times (C_S(R) - C_F), \tag{7}$$

where: D_L is the axial dispersion coefficient, ε the bed porosity, $C_S(R)$ is the bioactive compound concentration on the solid surface ($r = R$) in contact with the liquid phase, and v_s is the solvent velocity. The Danckwerts boundary condition is adopted at the column inlet Eq (8) [19].

$$D_L \times \frac{\partial C_F}{\partial z} = V_S \times (C_F - C_{IN}) \text{ at } z = 0, \tag{8}$$

where C_{IN} is the bioactive compound concentration in the solvent fed in the column. As the solvent used is pure inlet the column, assumed C_{IN} equal 0. At the packed-bed column outlet, the boundary condition adopted is Eq (9):

$$\frac{\partial C_F}{\partial z} = 0 \text{ at } z = H. \tag{9}$$

The axial dispersion coefficient (D_L) at the packed-bed extractor was approximated by the Peclet number correlation Eq (10) described by Chung and Wen [25], where *Re* is the Reynolds number Eq (11), *Pe* is the Peclet number Eq (12), ε_{BED} is the bed porosity, μ and ρ are the solvent viscosity and density, respectively. The solvent properties data (viscosity and density) were obtained from the software ASPEN PLUS 12.1™.

$$Pe = \frac{0.2+0.11\times Re^{0.48}}{\varepsilon_{BED}}, \tag{10}$$

$$Re = \frac{\rho\times V_s\times 2\times R}{\mu}, \tag{11}$$

$$Pe = \frac{V_s\times 2\times R}{D_L}. \tag{12}$$

2.4.3. Numerical solution

To describe the solid-liquid extraction in the packed-bed system, the model adopted is used to determine two phenomenological parameters: effective diffusion coefficient (D_{EF}) and external mass transfer (k_F). These parameters were estimated by comparing the experimental data and simulated data in terms of bioactive extraction yield (η), calculated by Eq (13):

$$\eta(\%) = 100 \times \frac{Q_F}{M_O} \times \int_0^t \big(C_F(z = H)\big) \times dt, \tag{13}$$

where: *Q* is the solvent flow rate (volumetric), *Mo* is the total amount of bioactive compounds present in yerba mate, and *H* is the total packed-bed length.

The first estimative of D_{EF} was taken with the predicted values of caffeine infinite-dilution diffusion coefficients (D_{AB}), estimated by the Wilke-Chang correlation [26], while the initial value of k_F was taken by Eq (14), where *Sh* is the Sherwood number Eq (15), and *Sc* is the Schmidt number Eq (16) [27]. These values are used as an initial guess for the optimization algorithm.

$$K_F = \frac{Sh\times D_{AB}}{2R}, \tag{14}$$

$$Sh = 0.442 \times Re^{0.69} \times Sc^{0.42}, \tag{15}$$

$$Sc = \frac{\mu}{\rho\times D_{AB}}. \tag{16}$$

2.5. Statistical analysis

The analysis of variance (ANOVA) was used to determine the impact of the experimental variables on the packed-bed extraction process. ANOVA followed by the Tukey test to compare the difference between the means of the samples at a 95% confidence level (*p-value* < 0.05) was adopted using StatSoft STATISTICA software (version 10.0).

The mathematical model adopted to estimate the mass transfer coefficient (k_F) and effective diffusivity in the solid phase (D_{EF}) was implemented using the open-source software Scilab 6.1.0. The numerical solution procedure and the computational algorithm were previously described and validated by Comerlatto et al. [19]. The relative mean error (*RME*) and coefficient of determination (R^2) were determined as the evaluation criteria for the mathematical model.

3. Results and discussion

3.1. Effect of temperature and feed flow rate on the extraction of bioactive compounds

Table 1 reports the global extraction yield and total phenolic concentration (TFC). In contrast, Table 2 reports the concentration of the most representative bioactive compounds evaluated during the packed-bed extraction. At 70 °C, the highest extraction yield was recorded during the 60 min packed-bed extraction process at the lowest feed flow rate (10 cm³/min), corresponding to almost 77% of the total amount of phenolic content predicted in the batch exhaustive extraction process. The concentration of the measured methylxanthines, theobromine, and caffeine, ranged from 21.0 × 10^{-2} to 53.5 × 10^{-2} mg/g_{YM} and 100.0 × 10^{-2} to 273.5 × 10^{-2} mg/g_{YM}, respectively, according to the packed-bed extraction conditions. The amount of the major phenolic acids (chlorogenic and caffeic acids) extracted ranged from 132.6 × 10^{-2} to 351.6 × 10^{-2} mg/g_{YM} and 57.0 × 10^{-2} to 156.3 × 10^{-2} mg/g_{YM}, respectively. The flavonoids extracted (rutin and quercetin) showed a concentration range of 35.4 to 128.5 × 10^{-2} mg/g_{YM} and 0.0428 to 0.088 × 10^{-2} mg/g_{YM}, respectively. The extraction yield obtained at the optimized condition, evaluated in CCD, was higher than 80%, except for quercetin, which resulted in about 78%.

Table 1. Central composite design (CCD) in the packed-bed extraction process: global yield and total phenolic extraction concentration.

Run	Temperature (°C)	Feed flow rate (cm³/min)	Extraction yield (%)	Total phenolic content (× 10^{-2} mg_{GAE}/g_{YM})
1	50	10	36.3 ± 0.3^{e}	448.6 ± 3.9^{e}
2	50	20	43.7 ± 0.3^{d}	539.9 ± 3.1^{d}
3	70	10	85.6 ± 0.7^{a}	1057.6 ± 8.7^{a}
4	70	20	82.1 ± 1.3^{b}	1014.4 ± 15.9^{b}
5	60	15	60.0 ± 1.8^{c}	741.4 ± 22.6^{c}
Ref	-	-	-	1235.7 ± 53.4

Note: Means with a different letter in the same column indicate statistical differences by Tukey's test ($p < 0.05$).

Several values of bioactive compounds extracted from yerba mate leaves were reported in the literature. Gerke et al. [14] in their study of the bioactive extraction process from yerba mate leaves in a batch process (70 g of yerba mate in 1.0 L of deionized water at 80 ℃ and stirring rate of 500 rpm) obtained nearly 69.0, 175.9, 845.4 and 1154.3 × 10^{-2} mg/g_{YM} of rutin, theobromine, chlorogenic acid and caffeine, respectively. Panzl et al. [4] extracted bioactive compounds from 25 different yerba mate samples, using a high-pressure extractor system (3 g of yerba mate processed with 500 mL of ultrapure water at 97 ℃ and 15 atm). As a result, the authors obtained concentrations of theobromine and caffeine ranging from 92× 10^{-2}–263 × 10^{-2} mg/g_{YM} and 565 × 10^{-2}–1367 × 10^{-2} mg/g_{YM}, respectively, according to the sample. Some differences between these results could be explained by the extraction process (e.g., solvent and temperature) and the source of the yerba mate sample. In general, phytochemicals content on yerba mate leaves is strongly susceptible to environmental conditions (e.g., soil, temperature, light intensity), genetic variability, industrial processing (dried – green mate, or roasted), and brewing conditions (infusion or use of heated or cold water) used in the preparation [10].

The effect of the process variables (temperature and feed flow rate) are evaluated by Analysis of Variance (ANOVA) and their effects and regression coefficients are shown in Supplementary File (Table S1). Temperature had a significant positive effect, i.e., raised temperature suggested an increase in extracted bioactive compounds. Furthermore, the feed flow rate did not show significance (except for total phenolic content and quercetin). Nonetheless, the interaction between temperature and feed flow rate exhibited significance and negative effect, wherein an increase in both variables led to a decrease in the extraction yield and quantity of the bioactive compounds extracted. Based on the data reported in Tables 1 and 2, the operational condition that led to the highest extraction yield and amount of extracted bioactive compounds was the temperature of 70 ℃; the feed flow rate had little influence at the evaluated level. This condition resulted in approximately 1057.6 × 10^{-2} mg_{GAE}/g_{YM} of total phenolic content (TPC) and 53.5 × 10^{-2}, 273.5 × 10^{-2}, 351.6 × 10^{-2}, 156.3 × 10^{-2}, 128.5 × 10^{-2}, and 88.3 × 10^{-2} mg/g_{YM} of theobromine, caffeine, chlorogenic acid, caffeic acid, rutin, and quercetin, respectively. Also, the total amount of phenolic concentration (1057.6 × 10^{-2} mg/g_{YM}) reported in Table 1 corresponds to almost 10% of the total expected for yerba mate, similar to what is reported in the literature [10].

Table 2. Central composite design (CCD) in the packed-bed extraction process: Concentration of the bioactive compounds evaluated.

Run	Theobromine (×10^{-2} mg/g_{YM})	Caffeine (×10^{-2} mg/g_{YM})	Chlorogenic acid (×10^{-2} mg/g_{YM})	Caffeic acid (×10^{-2} mg/g_{YM})	Rutin (×10^{-2} mg/g_{YM})	Quercetin (mg/g_{YM})
1	21.0 ± 0.1^{e}	100.4 ± 0.9^{e}	132.6 ± 1.1^{e}	57.0 ± 0.5^{e}	35.4 ± 0.3^{e}	42.8 ± 0.3^{e}
2	24.9 ± 0.1^{d}	125.4 ± 0.7^{d}	159.9 ± 0.9^{d}	69.0 ± 0.4^{d}	47.1 ± 0.4^{d}	55.9 ± 0.3^{d}
3	53.5 ± 0.4^{a}	273.5 ± 2.2^{a}	351.6 ± 2.9^{a}	156.3 ± 0.9^{a}	128.5 ± 1.1^{a}	88.3 ± 0.7^{a}
4	51.3 ± 0.8^{b}	262.2 ± 4.1^{b}	337.1 ± 5.3^{b}	149.9 ± 2.3^{b}	123.2 ± 1.9^{b}	84.6 ± 1.3^{b}
5	34.5 ± 1.1^{c}	169.9 ± 5.2^{c}	234.1 ± 7.1^{c}	105.1 ± 3.2^{c}	75.7 ± 2.3^{c}	69.6 ± 2.1^{c}
Ref.	58.4 ± 0.5	295.4 ± 2.4	387.3 ± 3.2	171.3 ± 1.4	143.9 ± 1.2	112.7 ± 0.9

Note: Means with a different letter in the same column indicate statistical differences by Tukey's test ($p < 0.05$).

Temperature is the main parameter that influences the packed-bed extraction process. At 10 cm³/min, it is possible to observe an increase in extraction yield from 36.3% to 85.6% when the temperature

was raised from 50 ℃ to 70 ℃ (Tables 1 and 2). The same behavior was observed for the feed flow rate of 20 cm³/min: An increase from 43.7% to 82.1% in extraction yield. Elevated temperatures exhibited a favorable impact in the context of solid-liquid extraction. This can be attributed to several factors, including reduced interactions between bioactive compounds and the solid matrix, enhanced solubility of bioactives, lowered solvent viscosity, and increased diffusivity of bioactive compounds within the solvent [28–30]. As reported by Zhong et al. [31], the caffeine solubility increased from 1.33×10^{-2} to 4.29×10^{-2} $g_{CAFFEINE}.g_{WATER}$ with the increase of solvent temperature from 15 ℃ to 55 ℃. Similarly, the solubility of theobromine followed the same behavior, increasing from 3.09×10^{-4} to 1.45×10^{-3} $g_{THEOBROMINE}.g_{WATER}$. It suggests that these bioactive compounds have an affinity with the solvent and higher is the chemical potential between the solid phase and solvent system at the highest temperature (enhancing the mass transfer process).

The solvent viscosity decreased from 5.14×10^{-3} Pa.s to 3.17×10^{-3} Pa.s when temperature increased from 50 ℃ to 70 ℃ (data obtained from ASPEN PLUS 12.1™), suggesting that the solvent has lower resistance to flow along the packed-bed (increasing the convective mass transfer) and also inside the porous solid particle (potential increase the effective intraparticle diffusion). The diffusivity also increased with the temperature. For example, the caffeine infinite-solute diffusion coefficient (D_{AB}) estimated by Wilke-Chang correlation is 1.71×10^{-9} m²/s at 50 ℃ and 2.23×10^{-9} m²/s at 70 ℃, i.e., an increase in of 23% in caffeine molecular diffusivity in water with this temperature increased. The higher the bioactive compounds' diffusivity, the higher the mass transfer rate from the solid matrix to the solvent promoting higher extraction yield at lower solid-liquid operational time.

The feed flow rate showed little significance in the packed-bed extraction process at the evaluated levels. From Table 1, it is observed an increase in the extraction yield of TPC (36.3 to 43.7%) when the feed flow rate was raised from 10 to 20 cm³/min at 50 ℃, while the TPC extraction yield decreased at 80 ℃ (86.5 to 81.2%). In this study, we observed the same behavior for the other bioactive compounds. Literature reports the importance of the feed flow rate in the packed-bed extraction processes, such as the supercritical fluids (SCF) and pressurized liquid extraction (LPE) systems [32,33]. The increase in the feed flow rate may improve the extraction process efficiency, at low temperatures, due to the increase in external mass transfer coefficient. The interstitial flow speed through the bed is directly related to the solvent flow rate. Consequently, with higher solvent flow rates, both the Reynolds and Sherwood numbers increase, leading to reduced external mass transfer resistance at the solvent-matrix interface. In this scenario, the more accessible bioactive compounds (at the solid surface) are extracted faster, resulting in a higher accumulated extraction yield at the end of the process [34,35].

However, at higher temperatures, the external mass transfer resistance becomes less relevant (due to the lower viscosity and higher solute diffusivity in the bulk solvent) and the leaching process is naturally faster, as previously explained. In this case, the higher the eluent solvent residential time inside the bed, the higher the solute leaching rate from the matrix solid. The residential time predicted for 10 and 20 cm³/min is 0.76 and 0.38 min, respectively, with the accumulated solvent volume of 600 cm³ and 300 cm³ after 60 min. This difference between the solvent contact time inside de packed bed and the amount of solvent that eluted the packed bed column in the operational time evaluated could explain the favorable condition to obtaining a higher accumulated extraction yield at the end of the packed bed extraction process.

3.2. Extraction kinetics of bioactive compounds

Figures 2 and 3 show the profile of TPC (mg g_{YM}^{-1}) and accumulated extraction yield are shown in for all experimental sets evaluated at the proposed CCD. The TPC was higher at the start of the process, resulting in an expressive initial extraction rate, but the extraction rate declined over time due to the lower bioactive concentration inside the solid matrix, reducing the potential driving force of the solid-liquid extraction [14,29]. The same behavior was reported in fixed-bed extraction systems, as SCF and LPE were applied in oil extraction from seeds [32], bioactive compounds from grains [35], and phenolic compounds from leaves [33]. At the central point (60 °C and 15 cm^3/min) the TPC in the aliquot measured at the operational time of 5 min was 492.4 × 10^{-2} mg/g_{YM}, resulting in an accumulated extraction yield of 31% of the TPC that is possible to extract with water at 60 °C. However, at the end of the assay, the TPC measured in the aliquot at 60 minutes was 7.17 × 10^{-2} mg/g_{YM}, resulting in an accumulated extraction yield of 60%, i.e., almost 50% of TPC recovery from yerba mate during packed-bed at the related condition was obtained in the first 5 min.

At the most effective operational condition (70 °C and 10 cm^3/100 min) the TPC obtained at 5 minutes was almost 505.0 × 10^{-2} mg/g_{YM}, corresponding to an extraction yield of 29.2% of the total TPC expected in the yerba mate evaluated in this study, while at the end of 60 min, the accumulated extraction yield was 85.6%. The TPC recovered at the first 5 min corresponds to almost 34% of the total amount extracted during all 60 min of the extraction process. These findings indicate that temperature elevation enhances the initial extraction rate by reducing the external mass transfer resistance and enhancing the bioactive solubility. Additionally, it improves the extraction rate during the extended extraction process due to increased molecular mobility within the solid matrix and decreased internal mass transfer resistance.

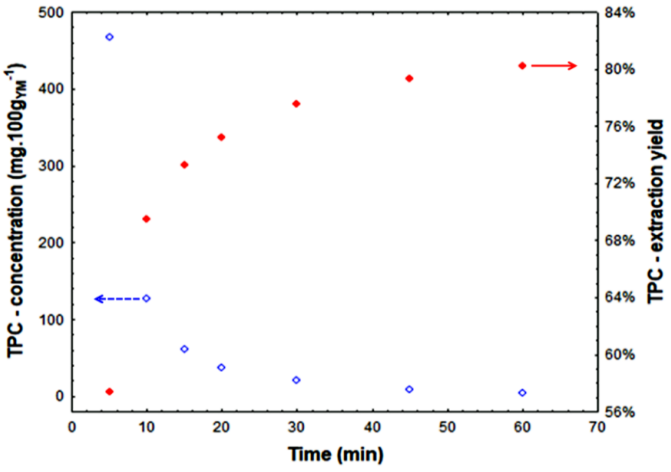

Figure 2. Packed-bed extraction kinetics for TPC at CCD central point: 60 °C and 15 cm^3/min. ●TPC-Extraction yield, ○ TPC-concentration (mg/100 g_{YM}).

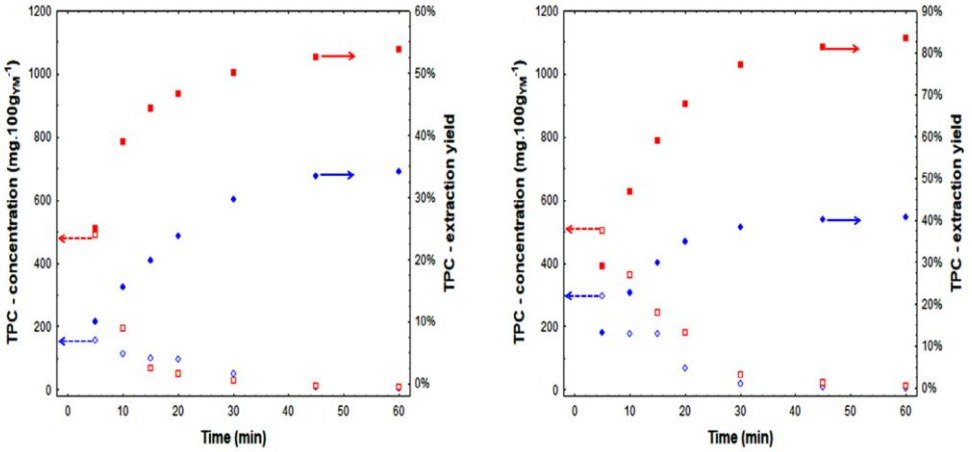

Figure 3. Packed-bed extraction kinetics for TPC at different temperatures (a) feed flow rate at 10 cm³/min, (b) feed flow rate at 20 cm³/min. ● TPC-Extraction yield at 50 °C, ◌ TPC concentration at 50 °C, ▪ TPC-Extraction yield at 70 °C, □ TPC-concentration at 70 °C.

Figure 4 shows the profile of extraction yield for caffeine. The kinetic behavior of the other bioactive compounds was similar to that of caffeine (supplementary file, Figures S1–S6) and likewise to that of TPC: high extraction rate at the beginning and fast extraction of bioactive compounds present on the solid surface (washing stage) followed by slow extraction stage and low extraction rate over time (usually limited by the intraparticle diffusion mass transfer). Quercetin showed the lowest extraction yield after 60 min, 70.1%, possibly due to its low amount extracted with water (at the exhaustive batch process: 112.7×10^{-4} mg/g_{YM}) and its lower water solubility (at 25 °C is reported that solubility of quercetin in water is nearly 3.86×10^{-5} $g_{QUERCETIN}.g_{WATER}$ [36]. Caffeine showed the highest extraction yield, the same way correlated with higher water solubility and the naturally higher amount present in yerba mate leaves. At 70 °C and 20 cm³/min, the initial extraction rate is higher than observed at 10 cm³/min and the same temperatures. As explained, a high feed flow rate improves the external mass transfer and this first stage resulted in higher initial extraction. After 30 min, the extraction rate is limited by internal mass transfer, and a low feed flow rate improves the residential time, which favors the solute diffusion from the internal solid matrix to the liquid phase.

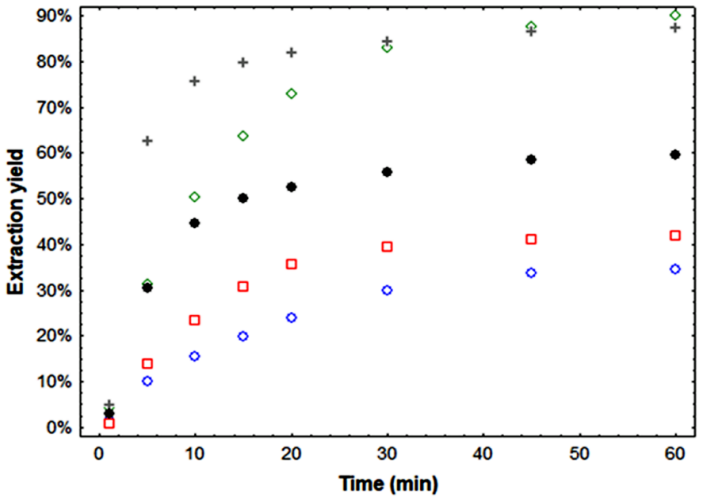

Figure 4. Kinetic of packed-bed extraction process for caffeine. ○ T = 50 ℃, Q = 10 cm³/min; □ T = 50 ℃, Q = 20 cm³/min; ● T = 60 ℃, Q = 15 cm³/min; ◊ T = 70 ℃, Q = 10 cm³/min; + T = 70 ℃, Q = 20 cm³/min.

In our study, experiments at 70 ℃ and 10 cm³/100 min, required 600 cm³ of the solvent to extract almost 21.0 mg.CAFFEIN from 8.0 g of yerba mate. This accounts for 88% of the total caffeine extracted from the same amount of yerba mate in an exhausted batch extraction process, which used 3000 cm³ of the solvent operating at a solid-liquid ratio of 8×10^{-2} g_{YM} g_{WATER} for 3 cycles, with a total operational time of 3 h. These results illustrate one of the advantages of using a packed-bed extractor over conventional solid-liquid extraction: In the solid-extraction batch process, the solvent remains in constant contact with the solid material. Over high operational periods, the saturated solvent attempts to extract more phenolic compounds from the initially low-content solid matrix. This reduced efficiency in recovering all bioactive compounds necessitates a sequential batch extraction process. Consequently, the results increased operational costs and a higher volume of solvent usage. For scaling up to industrial applications, the packed-bed extraction process could be suitable for extracting a high amount of phenolic compounds from a solid matrix, since the operational conditions and solvent system are well defined, the lower amount of required solvent over a conventional batch extraction process results in reduced operating costs [37].

3.3. Mathematical modeling of total phenolic concentration

Mathematical modeling has become an important tool for food manufacturers over the years for enhancing the quality of products and optimizing processes. Thus, the goal is to provide an output (concentration of bioactive compounds) based on an input data set (operational time) [20,38]. The modeling data obtained for the total phenolic concentration (TPC) from yerba mate are given below. Table 3 shows some physical and estimated properties used in the mathematical model evaluated, and Table 4 reports the model parameters of extraction kinetics.

Table 3. Physical properties in the mathematical model.

Property	Value	Source
Yerba mate particle size (m)	3.45×10^{-4}	Experimental
Yerba mate packed-bed length (m)	0.18	Experimental
Packed-bed diameter (m)	0.008	Experimental
Yerba mate density (kg/m^3)	1488.1	Experimental
Bed porosity	0.55	Eq (2)
Solvent density at 50 ℃ [kg/m^3]	969.1	Software ASPEN PLUS 12.1™
Solvent density at 60 ℃ [kg/m^3]	959.1	Software ASPEN PLUS 12.1™
Solvent density at 70 ℃ [kg/m^3]	949.0	Software ASPEN PLUS 12.1™
Solvent viscosity at 50 ℃ [Pa.s]	5.53×10^{-4}	Software ASPEN PLUS 12.1™
Solvent viscosity at 60 ℃ [Pa.s]	4.74×10^{-4}	Software ASPEN PLUS 12.1™
Solvent viscosity at 70 ℃ [Pa.s]	4.08×10^{-4}	Software ASPEN PLUS 12.1™
Caffeine infinite-solute diffusion at 50 ℃ [m²/s]	2.23×10^{-9}	Wilke and Chang [26]
Caffeine infinite-solute diffusion at 60 ℃ [m²/s]	1.86×10^{-9}	Wilke and Chang [26]
Caffeine infinite-solute diffusion at 70 ℃ [m²/s]	1.71×10^{-9}	Wilke and Chang [26]

Table 4. Modeling parameters for total phenolic content extraction from yerba mate leaves.

Parameters	50 ℃ 10 cm³/min	50 ℃ 20 cm³/min	70 ℃ 10 cm³/min	70 ℃ 20 cm³/min	60 ℃ 15 cm³/min
Superficial velocity (m/s)	6.63×10^{-3}	1.33×10^{-2}	9.95×10^{-3}	6.63×10^{-3}	1.33×10^{-3}
Mass transfer coefficient (m/s)	8.75×10^{-8}	1.94×10^{-7}	1.17×10^{-7}	1.77×10^{-6}	5.91×10^{-7}
Effective diffusion coefficient (m²/s)	9.34×10^{-11}	4.41×10^{-10}	2.14×10^{-9}	3.06×10^{-9}	1.11×10^{-9}
D_L (m²/s)	3.58×10^{-5}	6.60×10^{-5}	3.47×10^{-5}	6.34×10^{-5}	5.04×10^{-5}
Peclet Number	0.46	0.50	0.48	0.52	0.50
Biot Number	1.08×10^{-1}	5.04×10^{-2}	9.51×10^{-2}	6.64×10^{-2}	6.14×10^{-2}
Reynolds Number	29.15	58.31	38.72	77.44	50.48
coefficient of determination (%)	99.6	99.8	99.5	99.6	98.8
Relative mean error (%)	3.09	2.36	3.22	1.99	3.28

Figure 5 shows the simulated and experimental values of the extraction yield for TPC evaluated for experimental design (CCD). The mathematical model fits the experimental data very well, detecting that external mass transfer (washing stage) controls the solid-liquid mass transfer and the internal mass transfer limits the low extraction rate stage. As reported in Table 4, the multiscale mathematical model based on mass balance in solid and liquid phases proved to be highly accurate, with relative mean errors below 3.2% and coefficient of determination above 98.8%. The Peclet number exhibited values around 0.5 for all cases, suggesting that both axial dispersion and advection transport are significant, with dispersion being slightly more relevant for lower solvent flow rates [25]. It is also possible to observe that the Reynolds number falls within the interval 10–100 for all cases. For a packed bed filled with spherical particles, these values are usually considered in the transition regime from laminar to turbulent, therefore it is expected both dispersion and advection to be relevant. For a temperature of 70 °C, the Re number for a flow rate of 20 cm³ min^{-1} is significantly greater than for 10 cm³/min, indicating a smaller residence time of the solvent inside the column. As previously mentioned, this can be associated with a small reduction in the total yield for a higher flow rate.

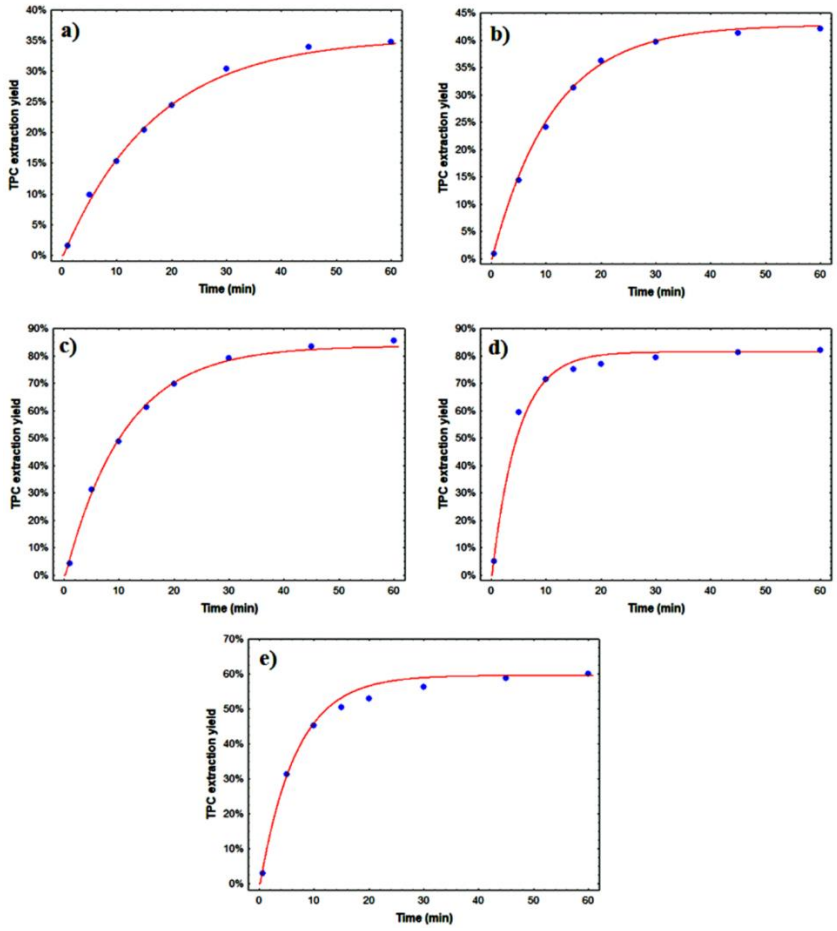

Figure 5. Comparison between the TPC extraction kinetic data and mathematical model. a) T = 50 °C, Q = 10 cm^3/min; b) T = 50 °C, Q = 20 cm^3/min; c) T = 70 °C, Q = 10 cm^3/min^{-1}; d) T = 70 °C, Q = 20 cm^3/min; e) T = 60 °C, Q = 15 cm^3/min. ● experimental data; ─ simulated data.

The Biot number showed values below 1, suggesting that external mass transfer is the major resistance during the extraction process. As observed in Figure 5, a significant quantity of bioactive compounds was extracted at the first 20 min (with a flow rate of 20 cm^3/min) a 30 min (with a flow rate of 10 cm^3/min) of the packed-bed extraction process. This behavior was expected because yerba mate leaves naturally store many bioactive compounds on their surface, as a physiological defense mechanism for the plant [2]. After the washing stage, only the bioactive compounds closely linked to solid morphology are available for extraction, resulting in solid-liquid extraction controlled by internal diffusion. Also, the morphology of the yerba mate leaves (previous gridding and small particle size) allows better contact and solubilization of bioactive compounds with the solvent, resulting in a reduced internal mass transfer resistance.

There are no reports about the mass transfer parameters using a packed-bed extraction system in the literature. Gerke et al. [14] estimated the intraparticle diffusion for chlorogenic acid and caffeine at the temperatures of 50 °C and 80 °C in the batch extraction process and these estimated values ranged from 1.8×10^{-12} to 1.2×10^{-11} m^2/s and 3.1×10^{-12} to 1.4×10^{-11} m^2/s, respectively. The results suggest that temperature significantly influenced the intraparticle diffusional coefficient.

Some variations in the intraparticle diffusion coefficient found in the literature, for similar samples, may be attributed to differences in the sample composition and morphology. Comerlatto et al. [19] observed intraparticle diffusion coefficients ranging from 1.8×10^{-12} to 1.2×10^{-11} m^2/s in the packed-bed extraction of soybean oil under various conditions, including temperature (30 ℃ to 50 ℃) and hydroalcoholic solvent mixtures (water-ethanol-isopropyl alcohol).

4. Conclusions

The results obtained in this study demonstrated that yerba mate leaves are a potential natural source of bioactive compounds and their large-scale extraction can be efficiently performed using a packed-bed process to obtain bioactive compounds with a reduced amount of solvent. The temperature significantly influenced the process, and the feed flow rate was relevant at low temperatures due to its positive effect on the external mass transfer. The maximum values of bioactive compounds recovered after 60 min were obtained at 70 ℃ and 10 cm^3/min, with concentrations of 8.83×10^{-2}, 53.5×10^{-2}, 128.5×10^{-2}, 156.3×10^{-2}, 273.5×10^{-2}, and 351.6×10^{-2} mg/g_{YM} of quercetin, theobromine, rutin, caffeic acid, caffeine, and chlorogenic acid, respectively. The kinetics study and the use of mathematical models provided a better understanding of the extraction process. These analyses indicated that the multiscale mathematical model predicted the solid-liquid mass transfer steps very well and showed the potential for scaling up the yerba mate extraction process in packed-bed extraction units for industrial applications.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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