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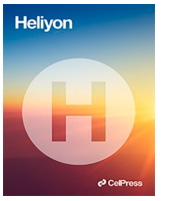

Three-zone simulated moving bed for the separation of chlorogenic acid and caffeine fractions in the liquid extract of spent coffee grounds

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ABSTRACT

Spent Coffee Grounds (SCG) is an agricultural residue obtained in a large quantity from local cafes in Thailand. In order to handle this waste effectively, the valorization of SCG is essential. SCG consists of beneficial phenolic compounds with antioxidative properties and caffeine, which can be recovered through extraction followed by separation and purification processes. In this work, water extraction of SCG was carried out. The volumetric composition of the liquid extract of SCG was then adjusted with an organic solvent, and the obtained mixture was used as the feed for subsequent separation. For the separation method of the SCG extract, a single chromatographic column was employed to separate a group of phenolic compounds (represented by chlorogenic acid) and a group of contaminants (represented by caffeine). The volumetric composition of the mobile phase was varied to determine the condition suitable for the separation of chlorogenic acid and caffeine in a C18 column. Adsorption parameters were determined and used to formulate the mathematical models describing the adsorption dynamics of those two bioactive compounds in the experimental breakthrough curves of standard solutions and the liquid extract of SCG. Furthermore, the three-zone simulated moving bed system (TZ-SMB) was designed to continuously separate fractions of chlorogenic acid and caffeine in the liquid extract of SCG. The adsorption parameters were employed in the optimization of TZ-SMB operating conditions using triangle theory, conducted via computer simulation. The experimental result of water extraction revealed that the yields of chlorogenic acid and caffeine were 0.292 and 0.583 mg/g dried SCG, respectively, using solid-to-liquid ratio of 1 g: 30 mL and temperature of 75 °C. The separation result in a single chromatographic column showed that the mobile phase consisting of acetonitrile, water, and formic acid (10: 90: 1.5 vol%) provided the linear adsorption isotherms for both chlorogenic acid and caffeine, and the chromatographic peaks of all compounds in the liquid extract of SCG were well separated. The simulated results of TZ-SMB at the optimal point revealed that the flow rates of desorbent, feed, extract product, and raffinate product were 0.626, 0.115, 0.081, and 0.593 mL/min, respectively, with the switching time of 20 min. At this point, the relative purities of caffeine in the extract product and chlorogenic acid in the raffinate product were 99.45 % and 98.88 %, respectively, with the maximum productivity of 0.045 mg/mL·h. In

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addition, for demonstration purposes, the lab-scale TZ-SMB experiment was conducted to show the separation of chlorogenic acid and caffeine in the liquid extract of SCG. The operating point from the triangle separation region was chosen based on the sensitivity of flow rate that ensured the criteria of purity. The experimental results showed that the relative purities of caffeine in extract product and chlorogenic acid in raffinate product were both 100 %, verifying the successful separation.

1. Introduction

The Bioeconomy, Circular Economy, and Green Economy, collectively known as the BCG model, have been implemented in Thailand to promote sustainable growth in the economy, society, and environment [1]. One of the primary objectives is to efficiently valorize biological resources by developing high-value-added products. This policy emphasizes the utilization of agricultural waste residues to maximize benefits. To achieve this goal, processes such as solid-liquid extraction (leaching), separation (isolation of product fractions), and purification (isolation of pure compounds) are employed to recover various products from biomass obtained through chemical and biological processes. Purified chemicals or biochemicals with high purities can serve as raw materials in the synthesis of high-value products, including cosmetics, nutraceuticals, and pharmaceuticals. Furthermore, the isolated contaminants can also be considered valuable by-products, contributing to the effective utilization of the overall manufacturing process.

Spent Coffee Grounds (SCG) is a biomass residue derived from the brewing process of coffee beans in beverage production. It has been generated in a large quantity every year due to the popularity of coffee drinks. According to the report by Choi and Koh [2], consumption of coffee about 120,000 tons can produce 96,000 tons of SCG. There has been a significant amount of research investigating the potential uses of SCG. For example, studies have reported that Spent Coffee Grounds contains phenolic compounds such as chlorogenic acid and gallic acid [3,4]. Phenolics are beneficial bioactive compounds known for their antioxidative properties and therapeutic effects, including anticancer, anti-inflammatory, and antimicrobial properties [4–6]. Chlorogenic acid is the primary bioactive substance found in SCG, with yields ranging from 51.72 to 213.98 mg/g, depending on the coffee species and extraction conditions [7]. In addition to chlorogenic acid, SCG also contains other compounds such as tannins and a significant amount of caffeine. Caffeine belongs to a group of alkaloids known as methylxanthines, which can affect the nervous system [8]. The yield of caffeine has been reported in the range of 3.19–6.67 mg/g, depending on the type of coffee [7]. When consumed in moderation, caffeine can stimulate the nervous system, keeping the body alert and reducing tiredness. However, excessive consumption can have negative effects on the body. Improper disposal of SCG in landfills can potentially lead to caffeine contamination in the ecosystem [3,9]. The use of SCG as a feed ingredient is limited due to its tannin content, which can result in reduced nutritional quality [6].

One efficient method of utilizing SCG is the extraction of remaining bioactive compounds using an environmentally friendly solvent, such as an ethanol solution [7,10]. The liquid extract of SCG contains phenolic compounds, particularly chlorogenic acid, and caffeine. Therefore, it is necessary to separate the phenolic compounds from caffeine to obtain high-purity phenolics that can be used as raw materials for nutraceutical and pharmaceutical applications. Earning high-purity compounds enables product development to achieve precise biological properties in the final product, free from the effects of impurities. Furthermore, considering the prices of biochemical standards, chlorogenic acid and caffeine with purities above 95 % are valued at 4600 and 200 Baht/g, respectively [11]. Consequently, implementing separation and purification processes to handle SCG extract is an appropriate choice for valorizing SCG waste.

Separation and purification processes for liquid mixtures can be carried out using chromatographic techniques. The principle is based on the adsorption of solutes on a solid adsorbent packed in the column [12]. During elution, each solute has a specific velocity while passing through the column, depending on its affinity or specific interaction with the solid adsorbent. This knowledge can be applied in batch separation equipment, such as preparative liquid chromatography, which is suitable for multi-component separations. However, this technique requires the use of large amounts of solvent, resulting in low product concentrations. Consequently, downstream processes incur high energy consumption to remove the solvent. Generally, the productivity is poor due to the low feed-to-adsorbent ratio [13]. To overcome this problem, the continuous separation system called simulated moving bed (SMB) was developed. It was first commercialized by Universal Oil Product (UOP). This system consists of multiple chromatographic columns connected in series, operating synchronously for both adsorption and desorption. There are four zones designed for adsorbent regeneration (Zone I), separation (Zone II), separation (Zone III), and eluent regeneration (Zone IV), respectively. Conventional SMBs can separate two groups of solutes with high purity, high concentration, and minimal solvent consumption. Therefore, the productivity of separation is significantly improved compared to batch chromatography. This technology has been applied in various fields, including petroleum, petrochemicals, carbohydrates, nutraceuticals, and pharmaceuticals [14,15].

The objective of this work was to develop a three-zone simulated moving bed (TZ-SMB) without Zone IV for the continuous separation of the phenolic compound fraction (represented by chlorogenic acid) and the contaminant fraction (represented by caffeine) in the liquid extract of SCG. The first part of this work focused on the separation method for the SCG extract, which was conducted in a single chromatographic column. The adsorption experiments of chlorogenic acid and caffeine were carried out to determine their adsorption parameters in the C18 column. Mathematical models were formulated to describe the adsorption dynamics of both substances in the breakthrough curve experiments. In the second part of this work, the obtained parameters and models were utilized to design and optimize the operating parameters of the TZ-SMB system, aiming for the highest possible productivity. The triangle theory was employed, and the separation performances were evaluated through computer simulation. Finally, to

experimentally demonstrate the separation of the chlorogenic acid fraction and caffeine fraction in the liquid extract of SCG, a lab-scale TZ-SMB system was utilized. One selected operating point from the triangle separation region was chosen to maintain purities of at least 98 % for both compounds while compensating for the flow rate fluctuations of all pumps in the TZ-SMB system.

2. Mathematical modelling

2.1. Adsorption dynamic in a single chromatographic column

The mathematical models describing adsorption dynamics in a single chromatographic column assume plug flow pattern of liquid stream. The liquid properties are constant. The adsorption operation is isothermal. Mass transfer mechanism involves convection and axial dispersion. The transfer of solute assumes linear driving force approximation. The material balance equations in liquid and solid phases are shown below [16,17]:

$$\text{Liquid Phase}: \frac{\partial C_i}{\partial \theta} + \gamma \frac{\partial \overline{q}_i}{\partial \theta} = \frac{\psi}{Pe} \frac{\partial C_i^2}{\partial \chi^2} - \psi \frac{\partial C_i}{\partial \chi} \tag{1}$$

$$\text{Solid Phase}: \frac{\partial \overline{q}_i}{\partial \theta} = \alpha_i \left(q_i^* - \overline{q}_i \right) \tag{2}$$

where C_i is the concentration of solute i in the liquid phase (g/L). q_i^* is the concentration of solute i in the solid phase (g/L), which is in equilibrium with the concentration of that in liquid phase. $\overline{q}_i$ is the average concentration of solute i in the solid phase (g/L). The dimensionless parameters are defined as follows:

$$\gamma = \frac{1 - \varepsilon_b}{\varepsilon_b} \text{ and } \psi = \frac{v t_s}{L_c} \tag{3}$$

$$Pe = \frac{v L_c}{D_{ax}} \text{ and } \alpha_i = K_{i,j} t_s \tag{4}$$

Dimensionless variables of time (θ) and column axial distance (χ) are written as:

$$\theta = \frac{t}{t_s} \text{ and } \chi = \frac{z}{L_c} \tag{5}$$

where ε_b is the external bed porosity. v is the interstitial velocity (m/s), defined as the ratio of superficial velocity to bed porosity. t_s is the operating time for adsorption-desorption operation (breakthrough curve experiment) or switching time for TZ-SMB operation (s). L_c is the column length (m). D_{ax} is the axial dispersion coefficient (m^2/s). Pe is Péclet number, representing the rate of convection to dispersion. $K_{i,j}$ is the global mass-transfer coefficient (s^{-1}) calculated from the equation shown below [18].

$$\frac{1}{K_{i,j}} = \frac{1}{k_i} + \frac{R_p}{3 k_{i,j}^f} H_i \tag{6}$$

where R_p is the radius of solid adsorbent (cm). H_i is the linear isotherm constant. k_i is the linear driving force mass-transfer coefficient (s^{-1}) calculated from the relationship proposed by Wilson and Geankoplis, as shown in Equation (7).

$$k_i = \left(\frac{\Omega D_{eff,i}}{R_p^2} \right) \left(\frac{1}{1 - \varepsilon_p} \right) \tag{7}$$

where

$$D_{eff,i} = \frac{\varepsilon_p D_{m,i}}{\tau} \tag{8}$$

$$\tau = \frac{\left(2 - \varepsilon_p\right)^2}{\varepsilon_p} \tag{9}$$

Where Ω is the geometric factor. $D_{eff,i}$ is the effective diffusivity (cm^2/s). ε_p is the particle porosity, which has the value of 0.694, obtained from our previous work [19]. τ is the tortuosity factor. The convective mass-transfer coefficient, $k_{i,j}^f$ (cm/s) for liquid phase, valid for $0.0015 <$ Reynolds number <55, can be expressed as shown in Equation (10) [20].

$$Sh = \left(\frac{k_{i,j}^f d_p}{D_{m,i}} \right) = \left(\frac{1.09}{\varepsilon_b} \right) \left(\frac{\rho_f v \varepsilon_b d_p}{\eta} \right)^{0.33} \left(\frac{\eta}{\rho_f D_{m,i}} \right)^{0.33} \tag{10}$$

The dimensionless number, Sh, is the Sherwood number. d_p is the diameter of adsorbent particles (cm). ρ_f is the density of solvent (kg/m^3). η is the viscosity of solvent (kg/m·s). The diffusivity of an adsorbed solute, $D_{m,i}$ (m^2/s), can be estimated using the correlation

of Wike and Chang, as written in Equation (11) [21,22].

$$D_{m,i} = 7.4 \times 10^{-8} \frac{(\varphi M_i)^{0.5} T}{\eta V_{m,i}^{0.6}} \tag{11}$$

where φ is the association solvent parameter [12]. M_i is the molecular weight of solvent (g/mol). T is the absolute temperature (K). $V_{m.i}$ is the molar volume of solute at its normal boiling point (mL/mol). The dimensionless initial and boundary conditions are written in Equations (12–14), respectively.

$$\text{Initial conditions} : C_i(\chi, 0) = 0 \text{ and } \overline{q}_i(\chi, 0) = 0 \tag{12}$$

Boundary conditions:

$$\text{At column entrance} : C_i(0, \theta) = C_i^{in} + \frac{1}{Pe} \frac{\partial C_i}{\partial \chi} \tag{13}$$

$$\text{At column exit} : \frac{\partial C_i}{\partial \chi}(1, \theta) = 0 \tag{14}$$

where C_i^{in} is the initial feed concentration of solute i fed to the column (g/L)

2.2. Thee-zone simulated moving bed system

The Three-zone simulated moving bed system, known as TZ-SMB [23,24], comprises three chromatographic columns interconnected in series. When each zone is equipped with a single column, it is referred to as the 1-1-1 configuration, as depicted in Fig. 1. This system is designed to achieve effective separation of different components. The specific roles of each zone is described as follow: the initial zone, denoted as zone I, is dedicated to adsorbent regeneration. It facilitates the desorption of all previously adsorbed solutes from the column, revitalizing the adsorbent for subsequent cycles. The primary purpose of zone I is to eliminate adsorbed solutes and prepare the column for subsequent separation cycles. Zones II and III serve as separation zones within the TZ-SMB system. Zone II focuses on adsorbing the more retained components, which exhibit a higher affinity for the adsorbent material. Conversely, zone III facilitates the desorption of less retained components, which have a lower affinity and can be readily eluted. The differential adsorption and desorption processes in zones II and III enable the effective separation of desired components from the mixture. It is worth noting that in comparison to the traditional four-zone SMB, the TZ-SMB eliminates zone IV, which is responsible for solvent regeneration. This exclusion results in a more diluted raffinate product and the absence of solvent recycling within the system. However, TZ-SMB offers several advantages, including lower pressure drop, reduced number of pumps and columns, and prevention of leakage. These benefits make TZ-SMB an attractive option for continuous separation processes, despite the trade-off of solvent dilution in the raffinate product.

The inlet streams of the TZ-SMB system consist of two main components: the desorbent, which serves as the carrier or mobile phase, and the feed mixture. The desorbent is responsible for facilitating the movement of solutes through the chromatographic columns, while the feed mixture refers to the liquid extract obtained from the solvent extraction process. On the other hand, the TZ-SMB system generates two outlet streams: the extract product and the raffinate product. The extract product predominantly contains the more

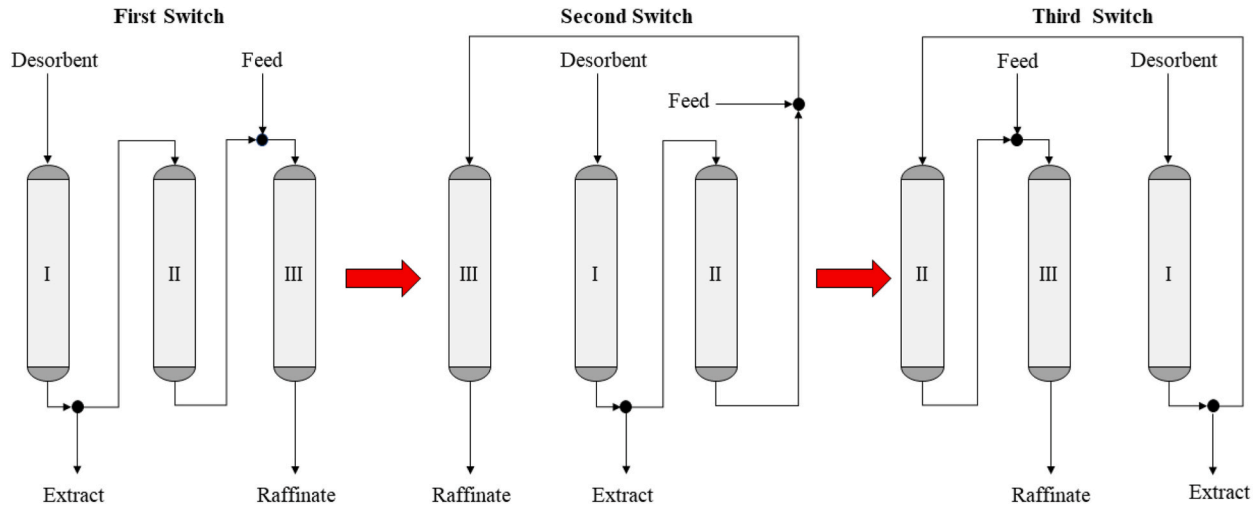

Fig. 1. Three-zone simulated moving bed system with 1 cycle operation.

retained component, which is strongly adsorbed on the adsorbent. In contrast, the raffinate product comprises the less retained component as the major component. All inlet and outlet streams are continuously fed into and withdrawn from the TZ-SMB system.

The operation of TZ-SMB follows a cyclical pattern, where all columns remain stationary, but the function of each column changes periodically along with the inlet and outlet ports. The relative position of the zones and ports remains constant throughout the operation. The desorbent is introduced at the entrance of Zone I to elute all adsorbed components as the extract product. The feed mixture is introduced at the inlet of Zone III, and the raffinate product is collected at the exit of this zone. The cycle time is divided into three steps, and the duration of each step is referred to as the switching time. After the switching time has elapsed, all inlets and outlets are moved in the direction of fluid flow, shifting by one column-position, while all columns in the system remain at rest. The movement of the inlet and outlet positions is facilitated by multi-position valves. This rotation of inlet and outlet positions is repeated three times, completing one cycle when the system returns to its initial position. This operation is the mimic of countercurrent flow between the solid phase and the liquid phase, which occurs in the true moving bed (TMB) operation. SMB can be performed without facing mechanical problems, such as erosions of adsorbent and column material caused by solid movement [14].

There are five operating parameters: desorbent flow rate (Q_D), feed flow rate (Q_F), extract flow rate (Q_E), raffinate flow rate (Q_R), and switching time (t_s). Assuming constant liquid density, the material balances of the TZ-SMB system can be written as shown in Equations (15)–(18).

$$\text{Overall balance} : Q_D + Q_F = Q_E + Q_R \tag{15}$$

$$\text{Zone I} : Q_I = Q_D \tag{16}$$

$$\text{Zone II} : Q_{II} = Q_I - Q_E \tag{17}$$

$$\text{Zone III} : Q_{III} = Q_{II} + Q_F = Q_R \tag{18}$$

where Q_j is the volumetric flow rate (mL/min) of zone j (j = I, II, and III).

For the assessment of separation performances, the calculated parameters, including the averaged concentrations (g/L) of chlorogenic acid (CGA) in the raffinate (R) and caffeine (CAF) in the extract (E) over the entire switching period of TZ-SMB, were obtained during the cyclic steady state. These parameters are expressed in Equation (19).

$$\langle C^R_{CGA} \rangle \text{ and } \langle C^E_{CAF} \rangle \tag{19}$$

The percentage of relative purities (%) of chlorogenic acid in the raffinate product and caffeine in the extract product are expressed as follows:

$$PU_R = \frac{\langle C^R_{CGA} \rangle}{\langle C^R_{CGA} \rangle + \langle C^R_{CAF} \rangle} \times 100 \text{ and } PU_E = \frac{\langle C^E_{CAF} \rangle}{\langle C^E_{CGA} \rangle + \langle C^E_{CAF} \rangle} \times 100 \tag{20}$$

The productivity of separation, expressed in mg/(mL·h), is defined as:

$$\text{Pd} = \frac{Q_F \left(C^F_{CGA} + C^F_{CAF} \right)}{(1 - \varepsilon_b) V_C N_C} \tag{21}$$

The production capacity (mg/h) of chlorogenic acid in the raffinate product is calculated as follows:

$$\text{Cap}_{CGA} = \langle C^R_{CGA} \rangle Q_R \tag{22}$$

The production capacity (mg/h) of caffeine in the extract product is calculated as follows:

$$\text{Cap}_{CAF} = \langle C^E_{CAF} \rangle Q_E \tag{23}$$

The solvent consumption ratio (mL/mg) is defined as follows:

$$\text{SC} = \frac{Q_D}{Q_F \left(C^F_{CGA} + C^F_{CAF} \right)} \tag{24}$$

where N_C is the number of columns in the TZ-SMB system. V_C is the column volume (mL). C^F_{CGA} represents the concentration (g/L) of chlorogenic acid in the feed solution. C^F_{CAF} represents the concentration (g/L) of caffeine in the feed solution.

3. Materials and methods

3.1. Experimental extraction of spent coffee grounds

3.1.1. Chemicals and Reagents

Spent Coffee Grounds (SCG), obtained from drip bag coffee, was used in this study. The standards of chlorogenic acid (HPLC grade) and caffeine (AR grade) were purchased from Sigma Aldrich. The organic solvents used for extraction and chromatographic methods were distilled deionized water (18.2 MΩ-cm), acetonitrile (HPLC grade, ACI LABSCAN), ethanol (AR and HPLC grades, Merck),

methanol (HPLC grade, ACI LABSCAN), formic acid (HPLC grade, Merck), and isopropanol (HPLC grade, ACI LABSCAN).

3.1.2. Pretreatment and water extraction of SCG

The drip bag coffee purchased from a local convenience store was used to make a cup of coffee by pouring 150 mL of hot water at 80 °C only once, following the provided instructions. The Spent Coffee Groundss were collected and vacuum-filtered to remove water for 1 h. Afterward, they were dried in an oven at 40 °C. Aqueous extraction of the dried Spent Coffee Groundss was conducted in a 1.5 mL tube, shaken at a speed of 1400 rpm in a controlled temperature shaker for 20 min. The extraction parameters were a temperature of 75 °C and a solid-to-liquid ratio of 1 g:30 mL. The obtained liquid extract was filtered using a 0.45-μm nylon filter membrane and sent for HPLC analysis to quantify the concentrations of chlorogenic acid and caffeine.

3.1.3. Analytical HPLC method

A high-performance liquid chromatography (HPLC) system from Knauer (Germany), consisting of a gradient pump, auto sampler, column oven, and DAD detector, was used to analyze the concentrations of chlorogenic acid and caffeine in the obtained liquid samples. The analytical column employed was a C18 column (4.6 × 250 mm, 10-μm particle size, from Phenomenex), kept in the oven at 40 °C. The mobile phase was a mixture of ACN: DI: formic acid in a volumetric ratio of 10:90:1.5 mL. The pump was operated in isocratic mode with a mobile phase flow rate of 0.6 mL/min. The injection volume of the collected samples was 50 μL. The wavelength of the UV detector was set to 280 nm. Calibration curves for both compounds were prepared in the range of 0.1–0.38 g/L. The analyzed concentrations were then used to calculate the yields of chlorogenic acid and caffeine, expressed in mg/g of dried Spent Coffee Grounds.

3.2. Separation of chlorogenic acid and caffeine in a single chromatographic column

The separation of chlorogenic acid and caffeine was studied through an adsorption experiment performed using an HPLC system (Knauer, Germany). The system consisted of an HPLC pump for delivering the mobile phase, an auto sampler, a column oven, and a UV detector. The chromatographic column employed was a C18 column from Phenomenex, with dimensions of 250 × 4.6 mm and a particle size of 10 μm.

3.2.1. Mobile phase selection

Several mobile phase solutions were tested to determine the elution characteristics of chlorogenic acid and caffeine. A standard solution of chlorogenic acid and caffeine, prepared at a concentration of 0.3 g/L, or the liquid extract of Spent Coffee Grounds (SCG), was injected into a C18 column. A mixture of acetonitrile (ACN), formic acid, and deionized water (DI) was used as the solvent, with volumetric ratios (in mL) of ACN: DI: formic acid as follows: 10:90:1.5 15:85:1.5, 20:80:1.5, 60:40:1.5, 70:30:1.5, and 80:20:1.5. The prepared solution was filtered using a 0.45-μm nylon filter membrane to remove any undesired particles that could cause clogging in the tube. The flow rate varied in the range of 0.1–1.0 mL/min, and the column temperature was maintained at 40 °C. The retention times of both substances were observed from the chromatogram upon elution. The suitable solvent as the mobile phase was evaluated based on the data obtained from the pulse injection experiment. The linear adsorption isotherm constants of chlorogenic acid and caffeine were calculated using Equation (25). The selectivity of the separation was calculated using Equation (26) [25].

$$t_{R,i} = \left[1 + \left(\frac{1-\varepsilon_b}{\varepsilon_b}\right) H_i\right] \left(\frac{L_C}{u_{int}}\right) \tag{25}$$

$$\alpha = \frac{H_{CAF}}{H_{CGA}} \tag{26}$$

where $t_{R,i}$ is the retention time of substance i (min). ε_b is the bed porosity, which is 0.35, as obtained from the previous work [26]. H_i is the linear adsorption isotherm constant of substance i. L_C is the column length (cm). u_{int} is interstitial velocity (cm/min).

3.2.2. Adsorption-desorption dynamics of chlorogenic acid and caffein in C18 column

The HPLC system was used to study the adsorption-desorption dynamics of chlorogenic acid and caffeine. The chosen mobile phase was used to prepare standard solutions of chlorogenic acid and caffeine in the range of 0.05–0.33 g/L, which were then used as the feed solution for the C18 column. The breakthrough curve experiments were carried out in two steps. During the adsorption step, the feed solution was passed through the column until the column reached equilibrium. Afterward, the desorption step was performed by feeding the chosen mobile phase into the column to elute all the adsorbed components. The flow rate ranged from 0.15 to 1 mL/min. The experiments were conducted with different concentrations of chlorogenic acid and caffeine in the feed solution. Additionally, the aqueous SCG extract solution (with prior concentration adjustment) was used as the feed solution for the breakthrough curve experiments. The volumetric ratio of the feed solution was acetonitrile: water (liquid extract of SCG): formic acid as 10:90:1.5 mL, respectively. The prepared feed solution and the column effluent, collected every 1 min, were analyzed for the concentrations of chlorogenic acid and caffeine using the HPLC conditions described in section 3.1.3.

3.2.3. Computer simulation of breakthrough curve experiments

The concentration-time profiles of chlorogenic acid and caffeine at the exit end of the column, obtained from the adsorption-

desorption experiments (breakthrough curves), were depicted using the mathematical models described in section 2.1. These models were utilized to tune-fit the experimental breakthrough curve data at various concentration levels in order to determine the adsorption parameters for each compound, including the linear adsorption isotherm constant, mass-transfer coefficient, and Péclet number. All equations were numerically solved using the finite element method in MATLAB® version 2021b and FLEXPDE® version 6.5, operating on the Windows® 10 operating system. The effectiveness of tune-fitting was evaluated by calculating the percentage average absolute relative deviation (%AARD) using Equation (27).

$$\mathrm{AARD} = \frac{100}{N_p} \times \sum_{i=1}^{N_p} \left| \frac{y_i^{\mathrm{sim}} - y_i^{\mathrm{exp}}}{y_i^{\mathrm{exp}}} \right| \tag{27}$$

3.3. Design of three-zone simulated moving bed (TZ-SMB) for the separation of chlorogenic acid and caffeine fractions using computer simulation

The five operating parameters of the TZ-SMB, namely the flow rates of desorbent, feed mixture, extract product, raffinate product, and switching time, were determined using the separation triangle theory, as detailed in section 4.3. The mathematical models describing the dynamic breakthrough curves in section 2.1 and the material balance of the TZ-SMB, as described in Equations (15)–(18), were employed with the previously determined adsorption parameters. Each operating condition within the separation triangle was used to simulate the concentration profiles of chlorogenic acid and caffeine along the column distance in each zone of the TZ-SMB, from the beginning until the cyclic steady state was observed. The system of equations was solved using MATLAB® version 2021b and FLEXPDE® version 6.5, running on the Windows® 10 operating system. Note that the inlet and outlet ports are periodically relocated to simulate the countercurrent flow between solid and liquid streams. This was achieved computationally by adopting the final state of each column as the initial state of the next column at the end of each switching period. The separation performances were evaluated using Equations (19)–(24) based on the data obtained during cyclic steady state. To simulate the operation of the TZ-SMB, the feed solution was defined as a mixture of chlorogenic acid and caffeine with initial concentrations of 0.032 g/L and 0.043 g/L, respectively. The column temperature was fixed at 40 °C. The desorbent flow rate and the switch time were fixed at 0.626 mL/min and 20 min, respectively. The optimal operating condition of the TZ-SMB was defined as the condition that maximized productivity while ensuring that the relative purities of chlorogenic acid in the raffinate product and caffeine in the extract product were both at least 98 %.

3.4. Experimental setup of three-zone simulated moving bed system for the separation of chlorogenic acid and caffeine fractions

The continuous separation apparatus, called a three-zone simulated moving bed (TZ-SMB) system, is shown in Fig. 2. It consists of

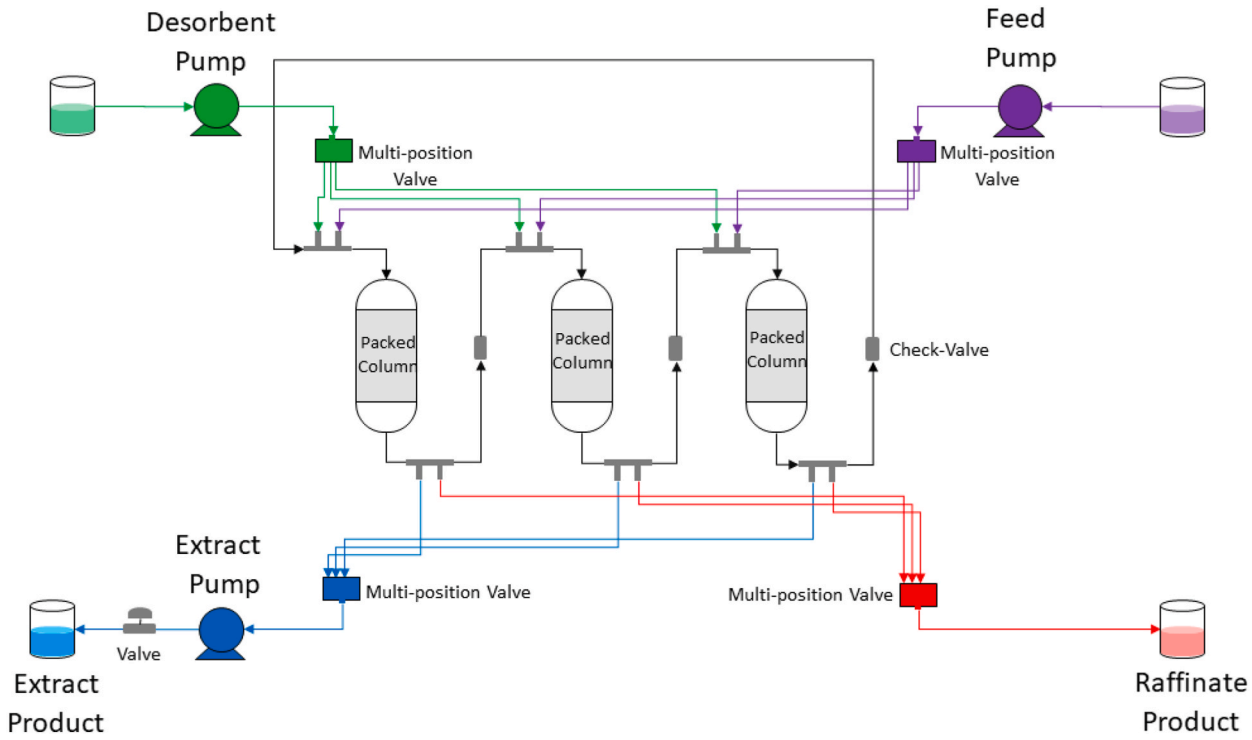

Fig. 2. Diagram of three-zone simulated moving bed (TZ-SMB) system.

three HPLC pumps (Shimadzu, Japan) for delivering the mobile phase, feed solution, and withdrawing the extract product. To perform the periodic port switching procedure of the TZ-SMB, four six-port valves (VICI Valco instruments) equipped with a control module are used. A needle valve and a metering valve are installed to control the flow rate of the extract product, while the flow rate of the raffinate product is freely set according to mass balance. Three C18 columns (4.6 × 250 mm, particle size of 10 μm, Phenomenex, USA) are placed in a controlled temperature convection oven at 40 °C. Three check valves are installed between the columns to control the flow direction. The feed solution for the TZ-SMB, which consisted of the liquid extract of SCG, was prepared as follows. For the extraction procedure, 10 g of pretreated Spent Coffee Grounds, as described in section 3.1.2, were mixed with 200 mL of deionized water. The extraction was conducted with agitation at 75 °C for 1 h. The resulting liquid extract (water phase) was filtered using a 0.45-μm nylon membrane and mixed with acetonitrile and formic acid at a volumetric ratio of ACN: DI: formic acid of 10: 90: 1.5 mL. The prepared feed solution was then sent for HPLC analysis to determine the concentrations of chlorogenic acid and caffeine. For the TZ-SMB operation, the flow rates of the desorbent, feed solution, extract product, and raffinate product were set as 0.626, 0.047, 0.101, and 0.572 mL/min, respectively. A switching time of 20 min was selected. The operation was performed for 60 switches (20 cycles). The extract and raffinate products were collected throughout the entire switching period and were sent for HPLC analysis to determine the concentrations of chlorogenic acid and caffeine. The separation performances, in terms of % relative purity, production capacity of the two bioactive compounds, and solvent consumption ratio, were evaluated using Equations (20)–(23), and (24) respectively.

4. Results and discussions

4.1. Aqueous extract of spent coffee grounds

It was reported that water was employed as the extracting solvent for polyphenols and polysaccharides from SCG [27]. Therefore, in this work water extraction of SCG was conducted to verify and identify the remaining bioactive compounds present in SCG, which were later used as the feed for separation in TZ-SMB. Normally, the volumetric composition of the feed (liquid extract) and desorbent (mobile phase) in TZ-SMB must be the same to maintain the separation behavior. In traditional ethanolic extraction, a high volumetric percentage of ethanol in the liquid phase can increase the viscosity of the solution. Consequently, high pressure drop occurs, leading to pipe and fitting leakages and causing mechanical damage to the adsorbent in the column. One way to avoid this problem is to evaporate the liquid extract to obtain the crude solid. After that, it can be dissolved in a mobile phase solution with lower viscosity, such as an acetonitrile solution. Therefore, in this work, the direct use of SCG aqueous extract solution is a promising approach since it can be immediately mixed with an organic solvent (acetonitrile) to obtain the appropriate volumetric ratio for the chromatographic separation. The excessive evaporation step of the liquid extract is consequently eliminated. Furthermore, according to the data of solubilities shown in Table 1, both chlorogenic acid and caffeine are soluble in water. This implies that water extraction is feasible even though the yields of chlorogenic acid might be lower and the yield of caffeine might be slightly higher when compared to ethanolic extraction.

Yields of chlorogenic acid and caffeine from water extraction of SCG, as described in section 3.1.2, are shown in Table 2. The ethanolic extraction (45 vol%) with the same extraction condition was also carried out for comparison. It was pointed out that the yield of chlorogenic acid using ethanol concentration of 45 vol% was 26.36 % higher than that of pure water extraction. This was due to the solubility of chlorogenic acid, which was higher in ethanol. Meanwhile, the yield of caffeine was 8.57 % lower. The solubility data of caffeine suggested that it can be dissolved well in water rather than in ethanol (see Table 1). Therefore, water extraction was likely considered comparable to ethanolic extraction.

The chromatograms of the aqueous extract and ethanolic extract (45 vol%) are shown in Fig. 3a and b, respectively. It is interesting to note that water extraction resulted in a reduction in the number of contaminants (more retained components or non-polar compounds), as observed from the smaller peaks I–V in Fig. 3a compared to those in Fig. 3b. The images of the ethanolic extract and water extract solutions are included in the corresponding chromatograms. It is important to mention that the color of chlorogenic acid is white to pale yellow. The ethanolic extract solution (Fig. 3b) appeared darker than the water extract solution (Fig. 3a), indicating the presence of impurities, as evidenced by the larger peaks I–V in Fig. 3b. The advantage of water extraction is that the peaks of the targeted compounds (chlorogenic acid and caffeine) were almost the same as those obtained using a 45 vol% ethanol solution, indicating a lower presence of impurities. Based on these results, water extraction of Spent Coffee Grounds is a reasonable method as it eliminates the need for an evaporation step and provides a suitable feed composition for the subsequent chromatographic separation performed in TZ-SMB.

The raffinate and extract products of TZ-SMB were determined based on the chromatogram of the water extraction of SCG (Fig. 3a). In the first separation step of TZ-SMB, the raffinate product was designated as the chlorogenic acid fraction, which included all peaks before the presence of caffeine. The extract product was assigned as the caffeine fraction, encompassing all peaks after caffeine. By

Table 1
Solubilities of chlorogenic acid and caffeine.

Compounds	Solubility in water	Solubility in ethanol	References
	mg/mL	mg/mL	
Chlorogenic acid	3.44	25	[28,29]
	Mole Fraction	Mole Fraction	
Caffeine	2.098×10^{-3}	1.713×10^{-3}	[30]

Table 2
Yields of chlorogenic acid and caffeine in SCG.

	Water extraction	Ethanolic extraction (45 vol%)	
Compound	Yield (mg/g Dried SCG)	Yield (mg/g Dried SCG)	% Difference (%)
Chlorogenic acid	0.292	0.369	+26.36 %
Caffeine	0.583	0.537	−8.57 %

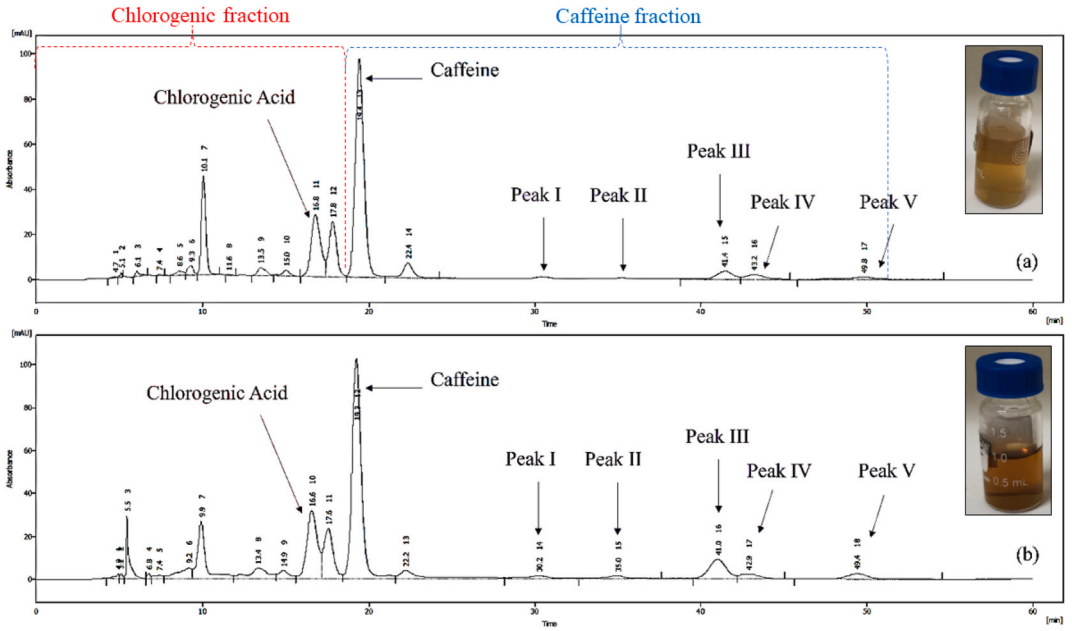

Fig. 3. Chromatograms of the extract solutions obtained using (a) water and (b) ethanol (45 vol%). The solid-to-liquid ratio was 1g:30 mL, and the extraction temperature was 75 °C.

disregarding the contaminants in the initial separation, TZ-SMB could be operated with a shorter switching time, allowing the system to reach cyclic steady state more rapidly.

4.2. Adsorption studies of chlorogenic acid and caffeine in a single chromatographic column

4.2.1. Selection of mobile phase

The chosen solution used as the mobile phase for separation in this work was an acetonitrile solution, which reduced the pressure built up compared to the case of an ethanol solution due to its low viscosity. The volumetric percentage of acetonitrile was varied as 10,

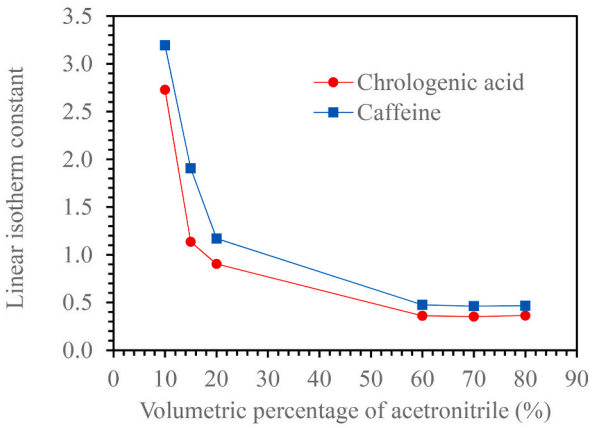

Fig. 4. Linear adsorption isotherms constants of chlorogenic acid and caffeine as a function of acetonitrile concentration.

15, 20, 60, 70, and 80 vol%. Additionally, the total time for HPLC analysis and the back pressure (read from the HPLC pump) were also taken into consideration. Standard solutions of chlorogenic acid and caffeine were used to determine the linear adsorption isotherm constant by means of a pulse injection experiment as described in section 3.2.1. The retention times observed from the chromatograms of both substances were used to calculate the adsorption isotherm via Equation. (25). The relationship between the linear adsorption isotherm constant of both compounds and the acetonitrile concentration in the mobile phase is represented in Fig. 4. Increasing the volumetric percentage of acetonitrile lowered the linear adsorption isotherm of both chlorogenic acid and caffeine. In other words, as the amount of water in the solution increased, chlorogenic acid and caffeine were more retained in the C18 column, as indicated by the relatively large values of their linear isotherms. When using a C18 column for separation, increasing the proportion of water in the mobile phase increased its polarity. Consequently, bioactive compounds with low polarity tended to adsorb strongly on the C18 adsorbent rather than being carried by the mobile phase.

According to Fig. 4, it is evident that the linear isotherm constant of caffeine is greater than that of chlorogenic acid, indicating that caffeine is the more-retained component in this system. Therefore, in TZ-SMB, caffeine is considered as the extract product, while chlorogenic acid is defined as the raffinate product. The selectivity of the C18 column, calculated using Equation (26), is defined as the ratio of the linear isotherm constant of caffeine to that of chlorogenic acid. A selectivity value greater than unity indicates that the C18 column favors the adsorption of caffeine over the other component. The results of the linear adsorption isotherm constants of both compounds in the standard solution (unary system) and in the liquid extract of SCG (multicomponent system) and the corresponding selectivity for various mobile phase compositions are presented in Table 3. The selectivity of the C18 column for the separation of chlorogenic acid and caffeine is greater than unity for all mobile phase compositions. These values range from 1.2 to 2.0, suggesting the feasibility of implementing TZ-SMB. It is noted that when the liquid extract of SCG was employed, the complexity of chromatographic system was more pronounced due to the presence of other impurities. However, in this case it was assumed that the synergistic or competitive effect play insignificant role because of low concentration of feed; therefore, the separation behavior was closely related to the unary systems, as observed from approximately the same value of H in Table 3. The chromatograms obtained from pulse injection experiments of SCG extract solution are shown in Fig. 5. The peaks become more well separated with an increasing volumetric percentage of water as observed from Fig. 5a–d. The ratio of acetonitrile, water, and acetic acid as 10:90:1.5 mL provided the best resolution for all peaks in the SCG extract (see Fig. 5d). Therefore, in this work the mobile phase consisting of acetonitrile, water, and formic acid in a ratio of 10:90:1.5 mL was chosen for TZ-SMB due to the high values of the linear adsorption isotherm constant (as represented in Table 3) and the observed effectiveness of separation in the chromatogram of the SCG extract (Fig. 5d).

4.2.2. Mathematical models describing adsorption dynamics of chlorogenic acid and caffeine in a single chromatographic column

4.2.2.1. Mono-component system. Adsorption studies of chlorogenic acid and caffeine were investigated via breakthrough curve experiments (as described in section 3.2.2) using a mono-component system. The first mobile phase selected was a mixture solution consisting of acetonitrile, water, and acetic acid in a ratio of 60:40:1.5 mL, respectively. Standard chemicals of chlorogenic acid and caffeine were dissolved in the mobile phase to prepare the feedstock solution. The concentration of chlorogenic acid was 0.12 g/L, while the concentration of caffeine was 0.4 g/L. The prepared solution was fed to the C18 column at a constant flow rate of 0.15 mL/min, and the column temperature was maintained at 40 °C. The product exiting the column was collected for HPLC analysis. The plots of effluent concentration against time, or breakthrough curves, for chlorogenic acid and caffeine are shown in Fig. 6a and b, respectively. Initially, the effluent concentration remained zero for a certain period of time, followed by a rapid increase in concentration. Subsequently, the concentration reached a plateau, indicating that the column had reached equilibrium, as evidenced by the relatively constant concentration. This concentration was approximately equal to the feed concentration. The break point, defined as the ratio of effluent concentration to the feed concentration equaling 0.5, occurred at 16 min for chlorogenic acid and 18 min for caffeine. This result confirms that caffeine was more strongly adsorbed compared to chlorogenic acid. In other words, chlorogenic acid was the less retained component and eluted from the column first. It is noteworthy that the shape of the breakthrough curve was nearly vertical, suggesting that the mass transfer resistance was minimal.

The simulated breakthrough curves of chlorogenic acid and caffeine, depicted by the black solid lines in Fig. 6, were generated according to the methodology outlined in section 3.2.3, employing the mathematical models described in section 2.1. The adsorption

Table 3
The linear adsorption isotherms constants (H) of chlorogenic acid (CGA) and caffeine (CAF) and the selectivity of C18 column as a function of mobile phase volumetric composition.

			Standard solution			Water extract of SCG		
Acetonitrile	DI Water	Formic Acid	H CGA.	H CAF.	Selectivity	H CGA.	H CAF.	Selectivity
(mL)	(mL)	(mL)	(−)	(−)	(−)	(−)	(−)	(−)
10	90	1.5	2.729	3.194	1.17	2.976	3.534	1.19
15	85	1.5	1.136	1.905	1.68	1.136	1.442	1.27
20	80	1.5	0.904	1.171	1.30	0.885	1.159	1.31
60	40	1.5	0.360	0.475	1.32	–	–	–
70	30	1.5	0.352	0.462	1.31	–	–	–
80	20	1.5	0.362	0.465	1.28	–	–	–

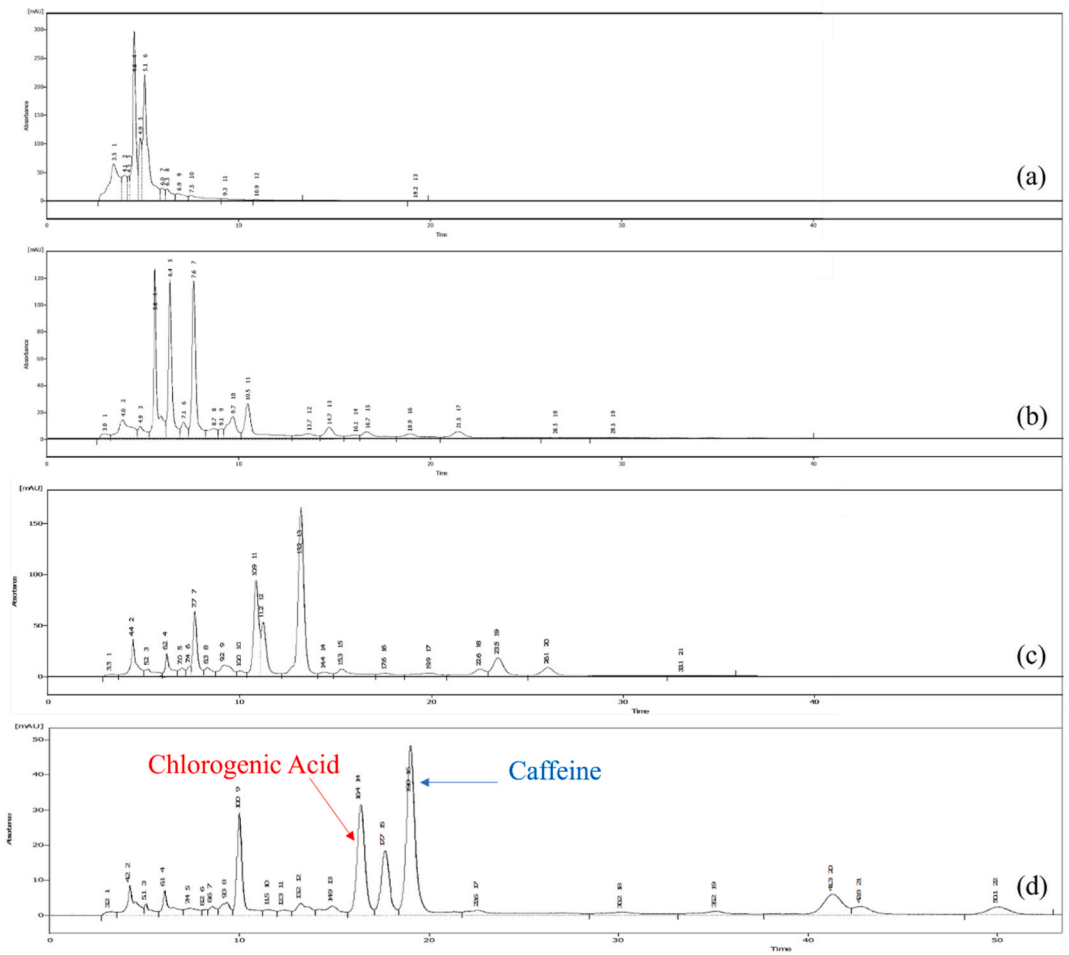

Fig. 5. Chromatogram of water extract of SCG using different acetonitrile concentrations in the mobile phase: (a) 40 vol%, (b) 20 vol%, (C) 15 vol%, and (d) 10 vol%.

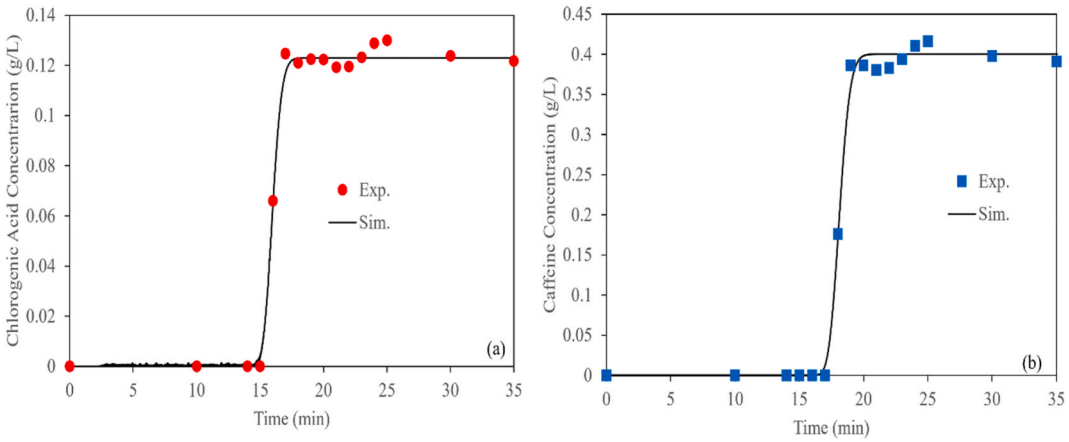

Fig. 6. Breakthrough curves of (a) chlorogenic acid and (b) caffeine in a mono-component system.

parameters considered were the linear adsorption isotherm (H), global mass transfer coefficient ($K_{i,j}$), Péclet number (Pe), and void fraction or bed porosity (ε_b). The initial estimates for the linear isotherm constants of both compounds were obtained from the values presented in Table 3. The initial estimates of the global mass transfer coefficient were computed using Equations (6)–(11). The fitted

parameters of the models are represented in Table 4. The obtained linear adsorption isotherms constants were close to those obtained from the pulse injection experiments shown in Table 3. The R-squared and % AARD values, indicating the goodness of fit of the model to the experimental data (experiment A), are summarized in Table 5. Apparently, the mathematical models represented the experimental data well, supported by the R-squared value of greater than 0.999 and low % AARD (less than 3.32 %).

4.2.2.2. Binary system. The adsorption parameters from the mono-component system were also tested with the binary mixture to validate some parameters with the data. The adsorption and desorption of chlorogenic acid and caffeine in a binary mixture, prepared from standard solutions, were investigated through breakthrough curve experiments. During the adsorption step, the solution mixture of both compounds with various inlet concentrations, as represented in Table 5 (experiments B–F), was fed to the column. The experimental conditions were the same as described in section 4.2.2.1. The breakthrough curves are depicted in Fig. 7 (a, c, e, g, and i). All compounds were adsorbed until the column reached equilibrium, as indicated by the concentration plateau. During the desorption step, as shown in Fig. 7 (b, d, f, h, and j), the mobile phase was fed to the column to elute all previously adsorbed components, as observed by the rapid decline in concentration. Eventually, the concentration reached zero, implying that the column was completely eluted. It was noted that, for each feedstock, there was a time gap for separation between the breakthrough curves of chlorogenic acid and caffeine during adsorption and desorption. This presented the feasibility for continuous chromatographic separation. The simulated breakthrough curves, as represented by the black solid lines, were constructed using the adsorption parameters obtained from the mono-component system. They were in good agreement with the experimental data of the binary system at different inlet concentrations of the mixture ranging from 0.1 to 0.34 g/L (experiments B–F in Table 5) with R-squared of 0.99 and AARD of less than 8.77 % for both compounds. Therefore, the models and adsorption parameters from the mono-component system were successfully validated.

4.2.2.3. Liquid extract of spent coffee grounds. The methodology for preparing the liquid extract of SCG as the feed to the column was mentioned in section 3.2.2. The composition of the selected mobile phase was a mixture of ACN: DI: Formic acid in a ratio of 10:90:1.5 mL (mobile phase II), as the peaks in the liquid extract of SCG were well-separated, as shown in Fig. 5d. The volumetric flow rate of the feed solution was 0.6 mL/min. The feed concentrations of chlorogenic acid and caffeine were 0.010 g/L and 0.016 g/L, respectively. The mathematical models were used to simulate the adsorption-desorption concentration profiles of chlorogenic acid and caffeine in the liquid extract of SCG in the breakthrough curve experiment. The experimental and simulated results of the breakthrough curves for both compounds are shown in Fig. 8a and b, respectively, for the adsorption and desorption steps. The fitted parameters of the breakthrough curves are represented in Table 4. The R-squared value and AARD of the fitting are shown in Table 5 (experiment G).

It was observed that the model was in good agreement with the experimental data. The separation time gap between the breakthrough curves of chlorogenic acid and caffeine was also noticed, resulting in the successful separation of the two compounds in the liquid extract of Spent Coffee Grounds. It was noted that the fitted Péclet number (*Pe*), representing the rate of convection to dispersion, was the same for all systems (mono and binary systems, and liquid extract) and type of mobile phases (I and III) as shown in Table 4, indicating the consistency of separation behavior. The fitted mass transfer coefficients (k_i) of both compounds for mobile phase II were of the same magnitude as those obtained for the case of mobile phase I. The parameters that markedly changed were the linear adsorption constants (H) of chlorogenic acid and caffeine, which were higher than those for the case of mobile phase I, as shown in Table 4. This resulted in a time shift of the breakthrough curves. The high water content in the mobile phase II (90 vol%) caused the solute to retain in the C18 column for a longer period of time.

For the validation of models and their corresponding adsorption parameters, another breakthrough curve experiment was carried out using the same experimental conditions of separation and liquid extract sample except that the feed flow rate was changed to 0.8 mL/min. The experimental and simulated breakthrough curves of both compounds are shown in Fig. 8c and d for adsorption and desorption steps, respectively. The goodness of fit, represented by R-squared value and % AARD are shown in Table 5 (experiment H).

Table 4
The fitted adsorption parameters from the breakthrough curve experiments.

	Mobile phase I ACN: DI: Formic acid = 60: 40: 1.5 mL		Mobile phase II ACN: DI: Formic acid = 10: 90: 1.5 mL	
	Standard solutions			
Parameter	Chlorogenic acid	Caffeine	Chlorogenic acid	Caffeine
Linear adsorption isotherm, H	0.348	0.468	–	–
Mass transfer coefficient, k (1/s)	187.986	233.921	–	–
Péclet number, *Pe*	1520	1520	–	–
	Liquid extract of Spent Coffee Grounds (SCG)			
	Chlorogenic acid	Caffeine	Chlorogenic acid	Caffeine
Linear isotherm constant, H	–	–	3.20	3.96
Mass transfer coefficient, k (1/s)	–	–	114.011	141.871
Péclet number, *Pe*	–	–	1520	1520
Column parameter				
Bed porosity	0.35			
Column diameter (m)	0.0046			
Column Length (m)	0.25			

Table 5
R-squared and %AARD values from the breakthrough curve experiments.

	Initial concentration (g/L)		R-squared		%AARD	
System	Chlorogenic acid	Caffeine	Chlorogenic acid	Caffeine	Chlorogenic acid	Caffeine
Mono-component system (Mobile phase I: ACN: DI: Formic acid = 60: 40: 1.5 mL)						
Experiment A	0.119	0.402	0.9989	0.9985	2.41	3.32
Binary system (Mobile phase I: ACN: DI: Formic acid = 60: 40: 1.5 mL)						
Experiment B	0.272	0.116	0.9992	0.9983	7.04	5.43
Experiment C	0.091	0.287	0.9989	0.9985	7.59	5.25
Experiment D	0.116	0.116	0.9980	0.9983	8.66	5.43
Experiment E	0.183	0.215	0.9981	0.9982	8.77	2.96
Experiment F	0.293	0.295	0.9985	0.9982	8.12	5.64
Liquid extract of SCG (Mobile phase II: ACN: DI: Formic acid = 10: 90: 1.5 mL)						
Experiment G	0.010	0.016	0.9972	0.9824	6.12	2.88
Experiment H	0.011	0.017	0.9877	0.9778	14.82	14.49

The models were still in good agreement with the experimental data. It was noticed that the breakthrough curves of both compounds were shifted to the left compared to those using the flow rate of 0.6 mL/min. The increase of the feed flow rate caused the system to equilibrate more rapidly for both substances.

4.3. The design and optimization of TZ-SMB for the continuous separation of chlorogenic acid fraction and caffeine fraction

For the continuous separation of chlorogenic acid and caffeine from liquid extract of Spent Coffee Grounds using TZ-SMB, the extract product was defined as the fraction consisting of caffeine as the majority, while the raffinate product was the fraction with high content of chlorogenic acid. This was in accordance with the experimental data in a single chromatographic column, revealing that caffeine was the more retained component, while chlorogenic acid was the less retained species. The operating parameters of TZ-SMB included switching time (t_s) and the volumetric flow rates of desorbent (Q_D), feed mixture or liquid extract (Q_F), extract product (Q_E), and raffinate product (Q_R). In order to determine the optimal condition of TZ-SMB, the constrains of optimization were first defined in terms of % relative purities of at least 98 % for chlorogenic acid in the raffinate product (PuR) and caffeine in the extract product (PuE), which were calculated from Equation (20). The criteria were satisfied by a set of conditions, which was screened for the maximum productivity (Pd), estimated from Equation (21). The objective function and constraints can be mathematically written as shown in Equations (28)–(30).

$$\text{Objective} : \text{Maximize Pd} \tag{28}$$

$$\text{Constraints} : \text{PuE} \geq 98\% \tag{29}$$

$$\text{PuR} \geq 98\% \tag{30}$$

In general, the desorbent flow rate (Q_D) and switching time (t_s) were first determined. Then to find the other three operating parameters (Q_F, Q_E, and Q_R), the separation triangle theory was employed along with the material balance. First, the flow rate ratio (m_j) in zone j (I, III or III) of TZ-SMB is written in Equation (31).

$$m_j = \frac{Q_j t_s - \varepsilon_b V_C}{(1-\varepsilon_b)V_C} \tag{31}$$

where Q_j is the volumetric flow rate in zone j (mL/min).

For complete separation of chlorogenic acid and caffeine at the end of switching time, the following conditions were required: (i) the flow rate ratio in zone I (regeneration zone) must be sufficiently high to elute all components from the column, especially caffeine which was the more retained species, (ii) the flow rate ratios in zones II and III (separation zones) must support the desorption of chlorogenic acid and adsorption of caffeine. These criteria can be written in the form of linear adsorption constants of chlorogenic acid (H_{CGA}) and caffeine (H_{CAF}) as follows.

$$\text{Zone I} : m_I > H_{CAF} \tag{32}$$

$$\text{Zone II} : H_{CGA} < m_{II} < H_{CAF} \tag{33}$$

$$\text{Zone III} : H_{CGA} < m_{III} < H_{CAF} \tag{34}$$

The separation triangle was constructed, as shown in Fig. 9, by varying the flow rate ratio in zones II and III according to the criteria defined in Equations. (32)-(34).

In theory, the area indicating the complete separation (100 % purity) is where the coordinate (m_{II}, m_{III}) is located within the triangle. The first step was to determine the flow rate ratio in zone I, m_I, and the switching time, t_s. The flow rate in zone I (Q_I or Q_D) must be sufficient to completely elute the more retained component (caffeine) out of the column, while maintaining the appropriate

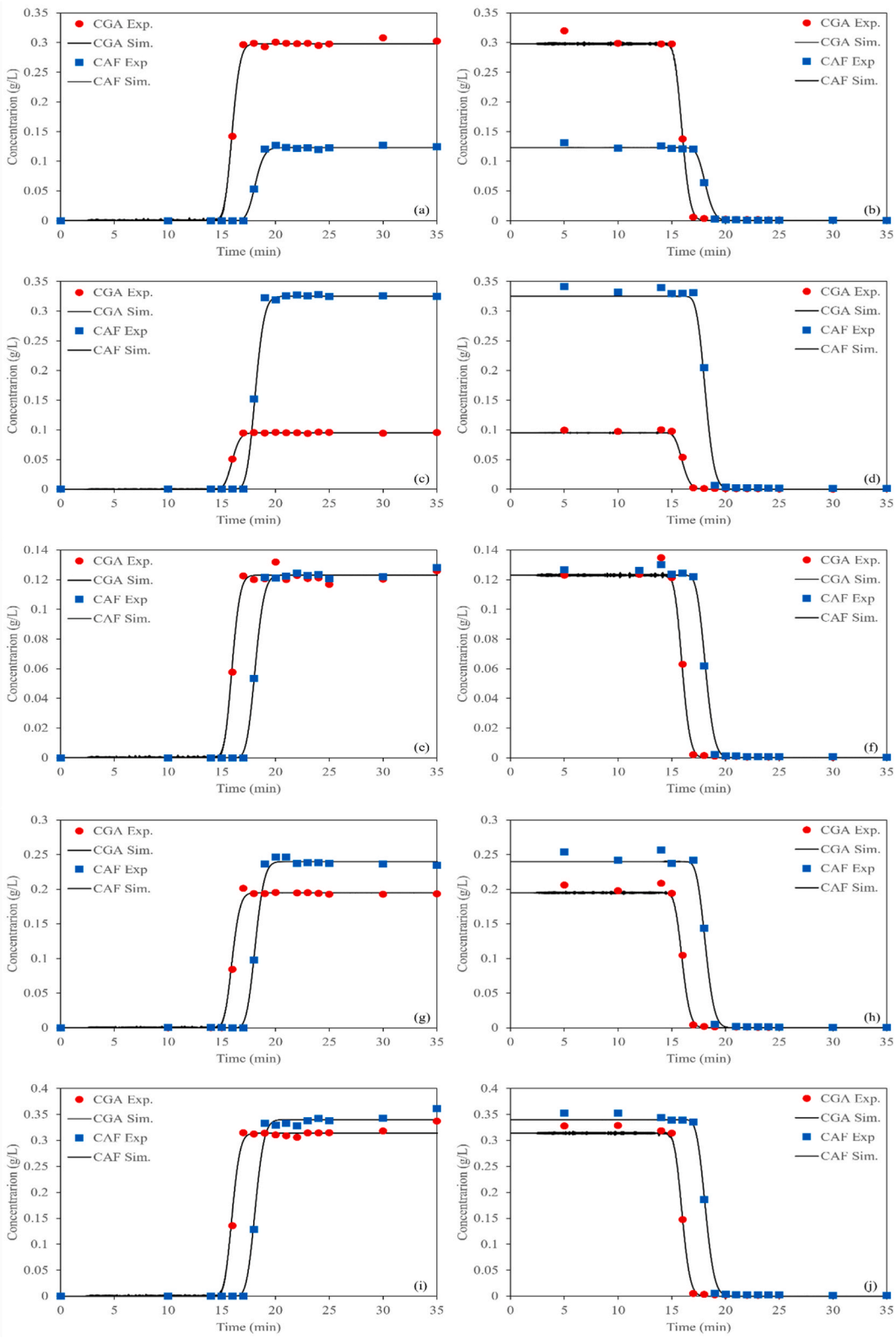

Fig. 7. Breakthrough curves of chlorogenic acid and caffeine in a binary system during adsorption and desorption steps.

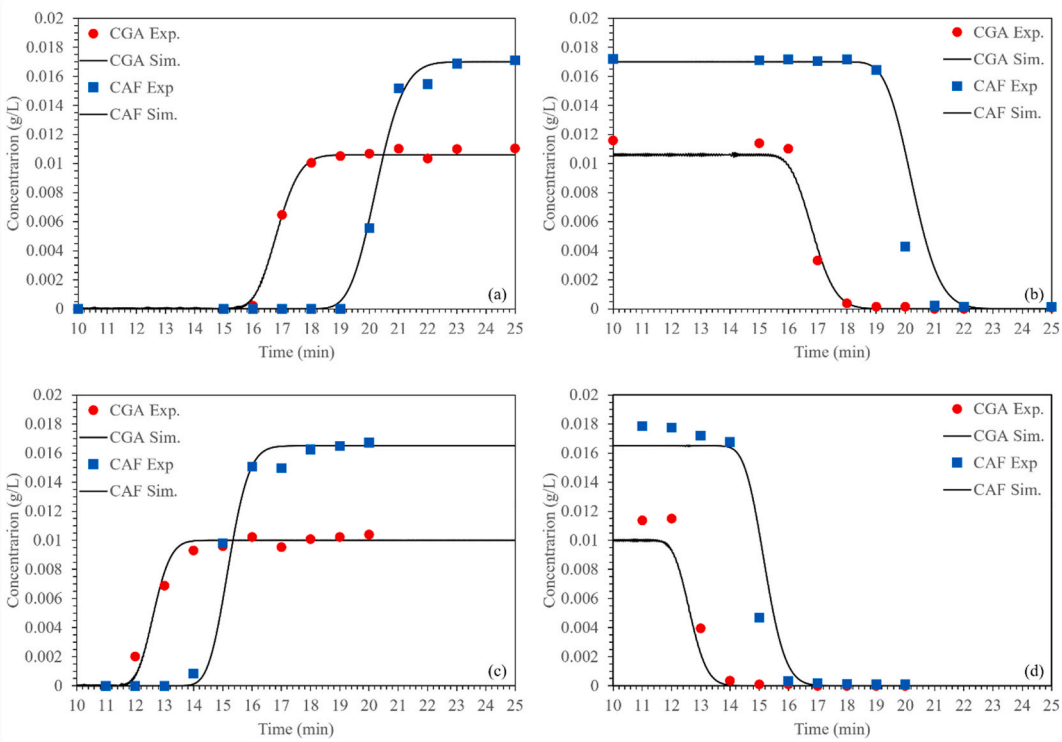

Fig. 8. The experimental and simulated breakthrough curves of chlorogenic acid and caffeine in the liquid extract of Spent Coffee Grounds (SCG) for the mobile phase flow rates of (a) 0.6 mL/min and (b) 0.8 mL/min.

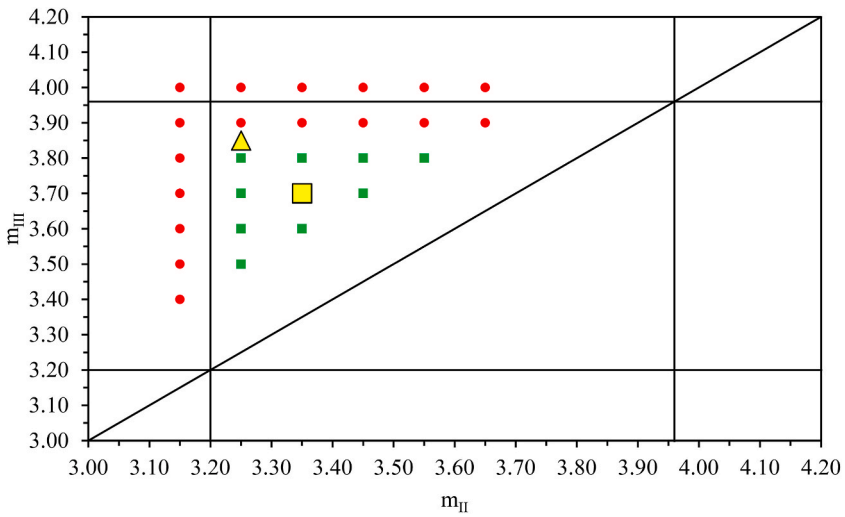

Fig. 9. The separation triangle for the separation of chlorogenic acid and caffeine. The red circle indicates the operating point at which the % relative purities of extract and raffinate products are less than 98 %; meanwhile, the green square represents the operating point at which the % relative purities are at least 98 %. The yellow triangle shows the point giving the maximum productivity. The yellow square is the point selected for the experimental demonstration of TZ-SMB. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

level of pressure drop. The desorbent flow rate was 0.626 mL/min, based on the experimental data of breakthrough curve during desorption. This corresponded to the flow rate ratio m_I of 4.1. For the switching period of TZ-SMB, the shorter the switching time, the faster the cyclic-steady state can be achieved. However, the small switching time can cause high flow rate in each zone of three-zone simulated moving bed. Extra caution on the safety and operational issues related to the pressure drop should be considered,

particularly for zone I, where the highest flow rate is used compared to the rest of the system. In this work the switching time of 20 min was used, since all species could desorb from the column within 20 min using this flow rate in zone I, judging from the breakthrough curve data during desorption as shown in Fig. 8b and d. The coordinate (mII, mIII) was varied within and on the boundary of the separation triangle, resulting in 27 simulation conditions represented by squares and circles marked on Fig. 9. The operating parameters of TZ-SMB for each simulation condition and the obtained simulated results of % relative purity of chlorogenic acid in the raffinate product and caffeine in the extract product, productivity, and capacity of TZ-SMB are shown in Table 6.

According to the simulated results in Table 6, the criteria of at least 98 % relative purity of chlorogenic acid in the raffinate product and caffeine in the extract product were satisfied by the conditions represented by the green squares in Fig. 9, while the red circles indicate the conditions with unsatisfied constraints. It was observed that those green squares formed a shape of triangle, which was smaller than the theoretical separation triangle constructed using Equations. (32)-(34). The explanation was that the large triangle assumed equilibrium between the solid and liquid phases without the effect of mass transfer resistance. The small triangle area accounted for the mass-transfer resistance, which usually occurs in the adsorption process. The simulated data of % relative purity of chlorogenic acid in the raffinate product (PuR), % relative purity of caffeine in the extract product (PuE), and productivity (Pd) were modeled using a second-order polynomial Equation (35). The R-squared values and root mean squared errors (RMSE) of the models are shown in Table 7.

$$Y = \beta_0 + \beta_1 m_I + \beta_2 m_{II} + \beta_{12}\, m_I\, m_{II} + \beta_{11} m_I^2 + \beta_{22} m_{II}^2 \tag{35}$$

Generally, the maximum feed flow rate is around the vertice of separation triangle. In order to accurately determine the optimal conditions, coordinates represented by black triangles were created in this area, as shown in Fig. 10a. Equation (35) was used to calculate the % relative purities (PuE and PuR) and productivity (Pd) by changing the coordinate of m_{II} and m_{III} in the separation triangle. The plot of PuE versus PuR was constructed to screen the conditions associated with % relative purities of at least 98 % for both products as shown in Fig. 10b. After that, the condition provided the maximum productivity was identified at the vertex of the triangle, marked as a yellow triangle in Figs. 9, 10a, and 10b. At this optimal condition of separation, as shown in Table 6, the flow rates of desorbent, feed, extract product, and raffinate product were 0.626, 0.115, 0.081, and 0.593 mL/min, respectively. The % relative purities of chlorogenic acid in the raffinate product and caffeine in the extract product were 98.88 % and 99.45 %, respectively. The productivity of TZ-SMB was 0.045 mg/(mL·h). The production capacity of chlorogenic acid and caffeine was 0.154 mg/h and 0.206 mg/h, respectively.

The plots of caffeine concentration in the extract product and chlorogenic acid concentration in the raffinate product against the number of switching are depicted in Fig. 11a and b, respectively. Note that the cyclical nature is not shown because each point

Table 6
Operating parameters of TZ-SMB and the simulated results for each condition in the separation triangle theory.

No	m_I	m_{II}	m_{III}	ts	Q_D	Q_E	Q_F	Q_R	%PuE	% PUR	Pd	CGA Cap.	CAF Cap.	Total Cap.
				(min)	(mL/min)	(mL/min)	(mL/min)	(mL/min)	%	%	mg/mL h	mg/h	mg/h	mg/h
1	4.10	3.15	4.00	20.00	0.626	0.128	0.115	0.613	95.36	91.65	0.064	0.207	0.278	0.485
2	4.10	3.15	3.90	20.00	0.626	0.128	0.101	0.599	95.01	97.63	0.056	0.180	0.256	0.437
3	4.10	3.15	3.80	20.00	0.626	0.128	0.088	0.586	94.41	99.34	0.049	0.155	0.226	0.381
4	4.10	3.15	3.70	20.00	0.626	0.128	0.074	0.572	93.49	99.81	0.041	0.129	0.191	0.319
5	4.10	3.15	3.60	20.00	0.626	0.128	0.061	0.559	92.29	99.91	0.034	0.103	0.157	0.261
6	4.10	3.15	3.50	20.00	0.626	0.128	0.047	0.545	90.39	99.93	0.026	0.076	0.121	0.197
7	4.10	3.15	3.40	20.00	0.626	0.128	0.034	0.532	87.70	99.93	0.019	0.050	0.088	0.137
8	4.10	3.25	4.00	20.00	0.626	0.115	0.101	0.613	99.48	92.05	0.056	0.193	0.243	0.436
9	4.10	3.25	3.90	20.00	0.626	0.115	0.088	0.599	99.47	97.70	0.049	0.168	0.222	0.390
10	4.10	3.25	3.80	20.00	0.626	0.115	0.074	0.586	99.43	99.45	0.041	0.141	0.189	0.330
11	4.10	3.25	3.70	20.00	0.626	0.115	0.061	0.572	99.39	99.84	0.034	0.116	0.157	0.273
12	4.10	3.25	3.60	20.00	0.626	0.115	0.047	0.559	99.32	99.94	0.026	0.089	0.121	0.210
13	4.10	3.25	3.50	20.00	0.626	0.115	0.034	0.545	99.24	99.96	0.019	0.065	0.087	0.152
14	4.10	3.35	4.00	20.00	0.626	0.101	0.088	0.613	99.96	90.49	0.049	0.169	0.209	0.378
15	4.10	3.35	3.90	20.00	0.626	0.101	0.074	0.599	99.96	97.61	0.041	0.142	0.187	0.329
16	4.10	3.35	3.80	20.00	0.626	0.101	0.061	0.586	99.96	99.40	0.034	0.117	0.157	0.274
17	4.10	3.35	3.70	20.00	0.626	0.101	0.047	0.572	99.96	99.86	0.026	0.090	0.121	0.211
18	4.10	3.35	3.60	20.00	0.626	0.101	0.034	0.559	99.95	99.95	0.019	0.065	0.088	0.153
19	4.10	3.45	4.00	20.00	0.626	0.088	0.074	0.613	99.99	90.22	0.041	0.142	0.173	0.315
20	4.10	3.45	3.90	20.00	0.626	0.088	0.061	0.599	100.00	97.49	0.034	0.117	0.153	0.270
21	4.10	3.45	3.80	20.00	0.626	0.088	0.047	0.586	100.00	99.46	0.026	0.090	0.120	0.210
22	4.10	3.45	3.70	20.00	0.626	0.088	0.034	0.572	100.00	99.87	0.019	0.065	0.087	0.152
23	4.10	3.55	4.00	20.00	0.626	0.074	0.061	0.613	100.00	87.62	0.034	0.117	0.137	0.254
24	4.10	3.55	3.90	20.00	0.626	0.074	0.047	0.599	100.00	97.32	0.026	0.090	0.117	0.208
25	4.10	3.55	3.80	20.00	0.626	0.074	0.034	0.586	100.00	99.39	0.019	0.065	0.087	0.152
26	4.10	3.65	4.00	20.00	0.626	0.061	0.047	0.613	100.00	86.61	0.026	0.090	0.099	0.189
27	4.10	3.65	3.90	20.00	0.626	0.061	0.034	0.599	100.00	97.13	0.019	0.065	0.082	0.147
Optimal	4.10	3.25	3.85	20.00	0.626	0.115	0.081	0.593	99.45	98.88	0.045	0.154	0.206	0.361

Table 7
Coefficients of second order polynomial equation for % relative purities and productivity.

Parameters	PuE	PuR	Pd
	(%)	(%)	mg/(mL·h)
β_0	−1165.000	−1037.000	0.0000
β_1	515.200	84.380	−0.0750
β_2	196.100	550.900	0.0750
β_{12}	−27.270	−31.240	0.0000
β_{11}	−59.020	4.967	0.0000
β_{22}	−13.590	−62.180	0.0000
R-squared	0.86	0.88	1.00
RMSE	1.47	1.62	0.00

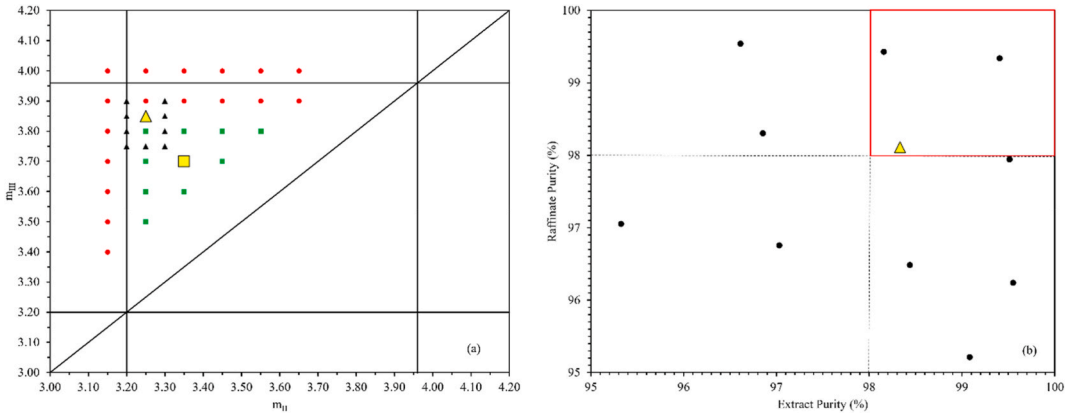

Fig. 10. (a) The plot of separation triangle with additional points represented by the black triangles and (b) The plot of % relative purities (PuE versus PuR) for the screening of operating conditions.

represents the time-average concentration of the entire period. It is apparent that the concentration of both compounds increases with time until they reach the cyclic-steady state condition. These conditions occur at the 35th switching (700 min) for the extract and at the 25th switching (500 min) for the raffinate. It is noticed that the concentration of caffeine in the extract is high without the presence of chlorogenic acid. On the other hand, the concentration of chlorogenic acid is the majority in the raffinate product with a relatively low amount of caffeine. Therefore, % relative purity of at least 98 % is achieved for both products of TZ-SMB.

It is noted that the concentration of chlorogenic acid in the raffinate product was relatively low (about 4.3 mg/L) compared to that in the feed solution (32 mg/L). This was because collecting the raffinate product for the entire period of switching time also includeed a large amount of mobile phase exiting the column at the beginning of each sample collection. Another suggestion is that the concentration of chlorogenic acid can be increased by discarding the product stream exiting the column for a certain period of time

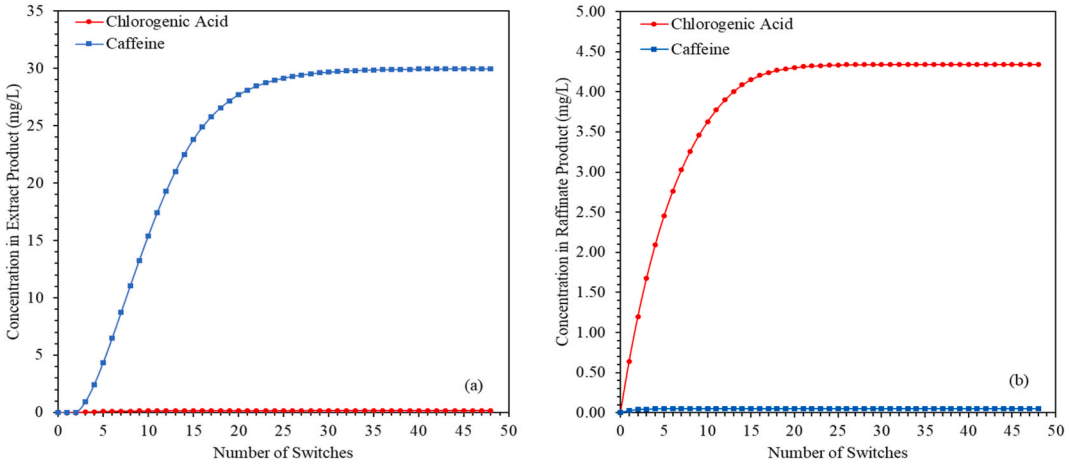

Fig. 11. Concentration-time profiles of chlorogenic acid and caffeine in (a) extract product and (b) raffinate product.

immediately after switching (when only solvent is present) before collecting the sample.

Fig. 12 shows the axial cyclic-steady state concentration profiles of chlorogenic acid and caffeine for each zone of TZ-SMB at different times: at the beginning of switching (t = 0) in Fig. 12a, at half of the switching period (t = 0.5ts) in Fig. 12b, and at the end of switching (t = t_s) in Fig. 12c. The concentration profile of both compounds formed a traveling wave from zone I to zone III (from left to the right) starting from t = 0 to t = t_s. At t = t_s (Fig. 12c), it was observed that the tailing edges of chlorogenic acid and caffeine concentrations passed the exit of zone I, implying that the desorbent flow rate in zone I was sufficient to desorb all components from the column. When this column became zone III, where the feed was introduced, upon the next switching, the chlorogenic acid in raffinate product was not contaminated with caffeine. In addition, the tailing edge of chlorogenic acid concentration wave almost passed the exit of zone II completely. In other word, the desorption of the less retained component was effective in this zone. Meanwhile, the rear edge of caffeine was still within this zone (zone II). The next switching changed this column into zone I, a large amount of caffeine trapped in the column was eluted as the main component in the extract product. Therefore, a complete desorption of chlorogenic acid from zone II would prevent the contamination of chlorogenic acid in the extract product. For complete separation (100 % purity), the fronting edge of caffeine concentration should be confined in zone III at t = ts, while a significant portion of chlorogenic acid concentration wave should have exited this zone. Therefore, the majority of raffinate product was chlorogenic acid and not contaminated by caffeine. For our optimal condition (at least 98 % purity of chlorogenic acid), a small portion of caffeine passed the exit of zone III, leading to small raffinate contamination.

4.4. The experimental demonstration of the separation of chlorogenic acid fraction and caffeine fraction from the liquid extract of SCG using a lab-scale TZ-SMB system

In the TZ-SMB system for the separation of chlorogenic acid and caffeine from the liquid extract of SCG, the extract product was defined as the caffeine fraction, with caffeine being the majority compound. On the other hand, the raffinate product was defined as the chlorogenic acid fraction, with chlorogenic acid as the majority component. The experimental condition chosen for the TZ-SMB demonstration was represented by the yellow square in Figs. 9 and 10a, corresponding to run number 17 in Table 6. This condition resulted in a lower productivity compared to the optimal condition; however, it was selected because it fell within the zone that provided high purities for both the extract and raffinate products, as indicated by the small triangle formed by the green squares. The reason for choosing this point was to maintain the purity standards of the products while taking into account potential flow fluctuations that could occur in a real system. The liquid extract, which was obtained following the preparation method described in section 3.4, was used as the feed in the TZ-SMB system. The concentrations of chlorogenic acid and caffeine in the feed were determined through HPLC analysis and found to be 3.09 mg/L and 7.49 mg/L, respectively.

The experimental and simulated results of the TZ-SMB at the 60th switch (20 cycles) are presented in Table 8. It is evident from the table that the percentage relative purities of chlorogenic acid and caffeine obtained from the simulation closely matched those obtained from the experiments. These results meet the criteria of at least 98 % purity. Fig. 13 displays the chromatograms of chlorogenic acid and caffeine in the feed, extract product, and raffinate product. Notably, the relative purity of caffeine in the extract product was found to be 100 %, which is consistent with the chromatogram of the extract product (Fig. 13b). This chromatogram indicates that only the peak corresponding to caffeine was observed, with no traces of chlorogenic acid. This outcome can be attributed to the complete desorption of chlorogenic acid and the adsorption of caffeine in zone II at the end of the switching time. In contrast, the raffinate product primarily consisted of the targeted chlorogenic acid with the initial impurities (all defined as a group of phenolics), and no traces of caffeine were observed, as depicted in the chromatogram in Fig. 13c. By comparing Figs. 13b and c to the chromatogram of the feed (Fig. 13a), it can be confirmed that the separation of the chlorogenic acid fraction and caffeine fraction was successful.

The experimental production capacities of chlorogenic acid and caffeine were 0.0090 and 0.0165 mg/h, respectively, which exhibited a slight deviation from the simulation results. It should be noted that these capacities were relatively low due to the low feed concentrations of both compounds, which were 3.09 and 7.49 mg/L, respectively. Therefore, in order to enhance the production capacity, it is necessary to increase the feed concentration. Additionally, apart from the feed concentration, the production capacity can be improved by increasing the feed flow rate. The feed flow rate should be adjusted to maintain mass balance with the other flow rates in the TZ-SMB system. In the case of TZ-SMB, the solvent to product ratio was determined to be 1259 mL/mg. This ratio is lower than that typically observed in batch separation processes such as preparative liquid chromatography, which consume a large amount of solvent compared to the quantity of feed input into the system. As a result, the utilization of TZ-SMB offers the advantage of reduced solvent consumption.

5. Conclusions

For the first part of this study, water extraction was conducted on Spent Coffee Groundss obtained from drip coffee to verify and identify the targeted phenolic compounds, mainly chlorogenic acid and caffeine. The yields obtained from water extraction were comparable to those obtained from ethanolic extraction (45 vol%). As a result, to simplify the downstream processing, water extraction was chosen as the method to prepare the feedstock for the separation experiments. In the second part of the study, the focus was on the separation process, specifically the investigation of adsorption dynamics in a single chromatographic column. The highest linear adsorption constants for both chlorogenic acid and caffeine were achieved using a mobile phase consisting of a ratio of 10:90:1.5 mL of acetonitrile, water, and formic acid, respectively. The mathematical models developed for the breakthrough curves showed good agreement with the experimental data for both chlorogenic acid and caffeine. These experimental data were obtained from both standard solutions and liquid extracts of Spent Coffee Groundss during the processes of adsorption and desorption.

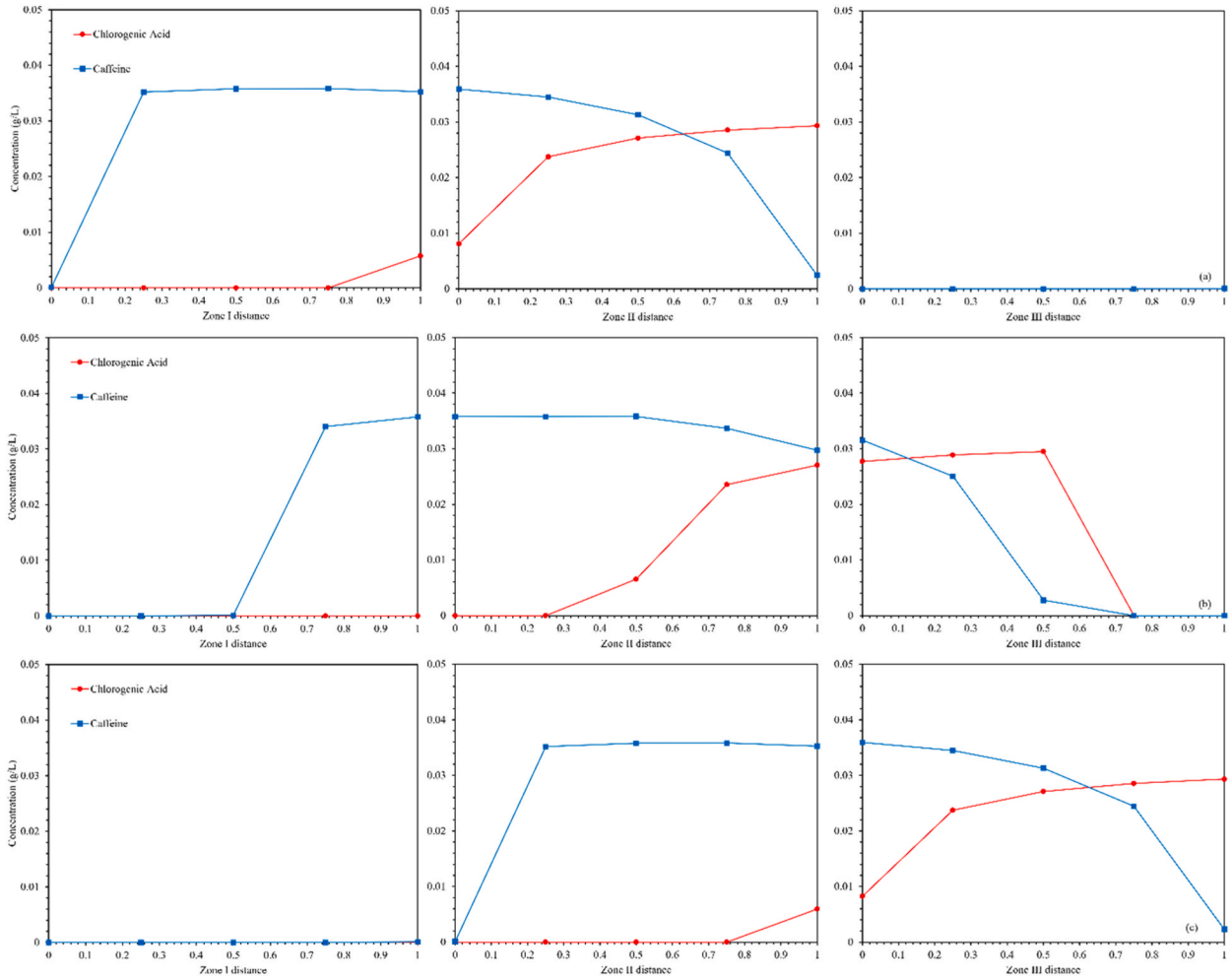

Fig. 12. Axial cyclic-steady state concentration profiles of chlorogenic acid and caffeine for zones I, II, and III of TZ-SMB at (a) t = 0 (b) t = 0.5t_s and (C) t = t_s.

Table 8
Experimental and simulated results of TZ-SMB at 60th switch (20 Cycles).

Parameters	Simulation	Experiment	% Deviation
Averaged concentration (mg/L)			
Extract product			
-Chlorogenic acid	0.001	0.000	–
-Caffeine	3.480	2.718	28.01
Raffinate product			
-Chlorogenic acid	0.254	0.262	2.80
-Caffeine	0.001	0.000	–
Relative purity (%)			
Chlorogenic acid in raffinate product, PuR	99.74	100	0.26
Caffeine in extract product, PuE	99.98	100	0.02
Capacity (mg/h)			
Chlorogenic acid in raffinate product, CGA Cap.	0.0087	0.0090	2.80
Caffeine in extract product, CAF Cap.	0.0211	0.0165	28.01
Solvent-to-product ratio (mL/mg)	1259		

The design and optimization of the TZ-SMB system were performed through computer simulations using the adsorption parameters obtained from the single column experiments. The optimal simulated result was achieved by setting the switching time to 20 min and the flow rates of desorbent, feed, extract, and raffinate to 0.626, 0.115, 0.081, and 0.593 mL/min, respectively. This configuration yielded a relative purity of 99.45 % for caffeine in the extract product and 98.88 % for chlorogenic acid in the raffinate product. The

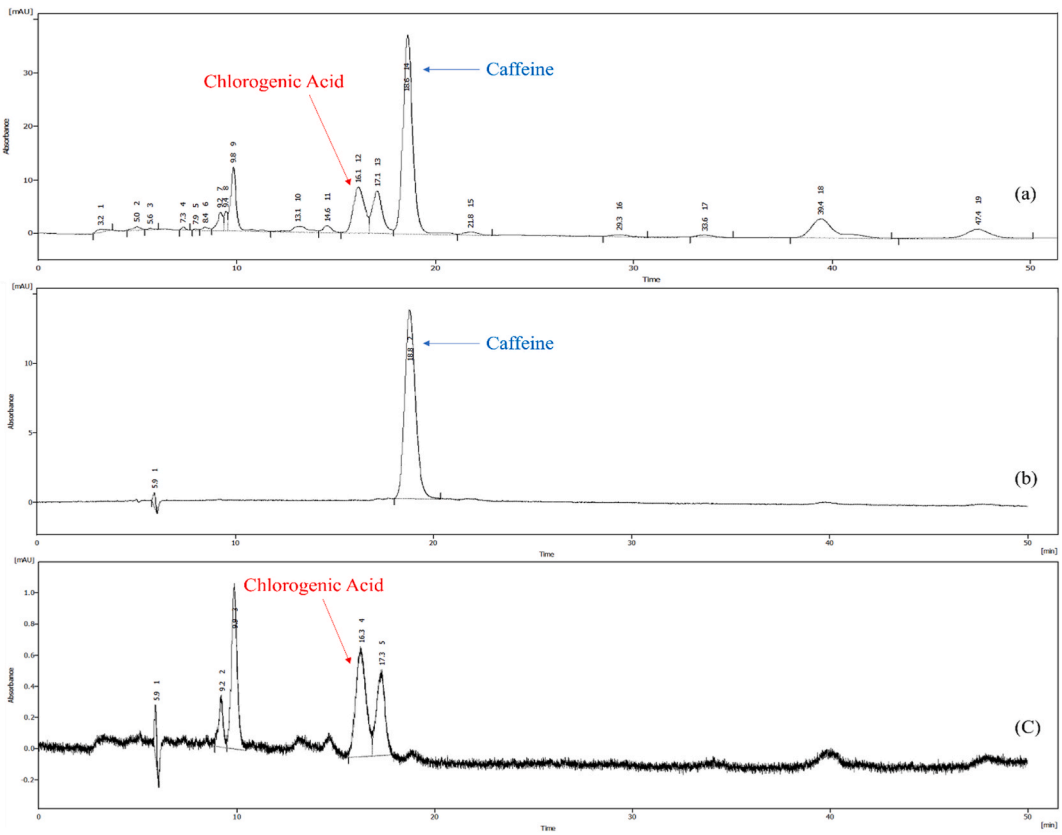

Fig. 13. Chromatograms of chlorogenic acid and caffeine in (a) the feed of TZ-SMB, (b) the extract product, (c) the raffinate product at 60th switch (20 Cycles).

maximum productivity achieved was 0.045 mg/(mL·h). Experimental demonstrations of the TZ-SMB system were conducted using a switching time of 20 min and flow rates of desorbent, feed, extract, and raffinate set to 0.626, 0.101, 0.047, and 0.572 mL/min, respectively. The experimental results demonstrated that the production capacities for caffeine and chlorogenic acid were 0.0165 and 0.0090 mg/h, respectively. The relative purities of caffeine in the extract product (caffeine fraction) and chlorogenic acid in the raffinate product (chlorogenic acid fraction) were both 100 %, indicating a complete separation of these two groups. The solvent consumption ratio was determined to be 1259 mL/mg, showcasing the potential for reduced solvent usage in the separation process.

As a suggestion and recommendation, to obtain a high purity of chlorogenic acid separated from the crude extract, the raffinate product, which contains a mixture of chlorogenic acid and other impurities, can be used as the feed in a second round of TZ-SMB separation. This would allow for the isolation of only chlorogenic acid as the extract product while discarding the impurities as the raffinate product.

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Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Preuk Tangpromphan: Conceptualization, Methodology, Resources, Visualization, Writing – original draft, Writing – review & editing, Investigation. **Supaphorn Palitsakun:** Resources, Writing – original draft. **Attasak Jaree:** Conceptualization, Formal analysis, Methodology, Resources, Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing 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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