Results in Engineering 17 (2023) 100914

Contents lists available at ScienceDirect

Results in Engineering

journal homepage: www.sciencedirect.com/journal/results-in-engineering

Solubilization of eugenol from *Piper betle* leaves to supercritical carbon dioxide: Experimental and modelling

Nur Husnina Arsad [a], Nicky Rahmana Putra [a,*], Zuhaili Idham [a], Nur Salsabila Md Norodin [a], Mohd Azizi Che Yunus [a], Ahmad Hazim Abdul Aziz [b,**]

[a] *Centre of Lipid Engineering and Applied Research (CLEAR), Ibnu Sina Institute for Scientific and Industrial Research, Universiti Teknologi Malaysia, 81310, Johor Bahru, Malaysia*
[b] *Faculty of Food Science and Nutrition, Universiti Malaysia Sabah, Kota Kinabalu, 88400, Malaysia*

A R T I C L E I N F O

Keywords:
Piper betle
Eugenol
Supercritical carbon dioxide
Solubility
Modelling

ABSTRACT

Piper betle leaves, which contains a high level of eugenol, is abundantly grown and distributed in many Asian countries. Eugenol is an important principal phytochemical found in betel leaves. This study proposed to determine the solubilization studies of eugenol in supercritical carbon dioxide from piper bettle leaves. The variables were pressure of 10 MPa–30 MPa, temperature of 40 °C–70 °C and flow rate of 4 mL/min to 8 mL/min. In solubility study, the Chrastil model offered the best fitting to correlate the solubility data of *Piper betle* leaves extract with the lowest average absolute relative deviation (AARD) of 6.20%. The coefficient values of k for solubility of extract at flow rate of 4, 6 and 8 mL/min were −0.27, 0.17 and 0.16, respectively. Furthermore, the coefficient values of k for solubility of eugenol at flow rate of 4, 6 and 8 mL/min were −0.25, −0.15 and −0.05, respectively. It is hence believed that the solvation power of SC-CO$_2$ was higher at high flow rate to increase the solubility of *Piper betle* leaves extract and eugenol.

1. Introduction

Medicinal plants play a golden role by providing for use as cosmetic substances, source of food, and ancient medicines. Undoubtedly, these plants should be employed in the discovery of a more natural, sustainable, and affordable source of medication in the primary health care system due to the wide diversity of bioactive compounds [1]. The leaves are recognized as “Green Gold” due to its colour and it is widely used in Malaysia, Thailand, India, Sri Lanka, Taiwan and others southeast Asian countries especially in the improvement of oral health [2,3]. Given that it is a cheap and readily accessible plant, various parts of the *Piper betle* plant are used in traditional medicine for treatment of several conditions such as constipation, conjunctivitis, itches, rheumatism and abrasions [4]. It has been suggested that the main compound that contributed to its medicinal properties was Eugenol [5].

Eugenol is a phenylpropene, an allyl chain-substituted guaiacol and a member of the phenylpropanoids class of chemical compounds with colourless to pale yellow oily liquid [6]. This fairly soluble in water and organic solvents which can categorized as a slightly polar compound. Eugenol is considered as versatile molecule used as an ingredient in various products including pharmaceutical, food industry, fragrance, flavour, cosmetics [7,8]. To date, the food industry is moving towards the application of eugenol in food preservation owing to its antimicrobial properties. The rise in foodborne diseases worldwide also have been driving the demand for eugenol to be used as ingredients effective preservation strategy [9]. Thus, an effective extraction process for eugenol production is important in ensuring that this compound is feasible to its clinical or pharmaceutical application.

Separation procedures are critical in the processing of biomaterials. Because the density of supercritical fluid is closer to that of liquids and its viscosity is low, equivalent to that of gases, it exhibits ideal transport qualities that boosted its adaptability as a solvent for liquid extraction procedures [10,11]. As a result, supercritical fluid extraction (SFE) technology has been used to improve high-quality products and reduce the amount of solvent required, where the supercritical fluid’s high density contributes to a high diffusivity equivalent to that of liquids, resulting in faster solute particle dissolution in solvent [12,13]. Thermally labile, lipophilic, non-volatile biological products are frequently

---

* Corresponding author.
** Corresponding author.
E-mail addresses: rahmana@utm.my (N.R. Putra), hazim.aziz@ums.edu.my (A.H. Abdul Aziz).

https://doi.org/10.1016/j.rineng.2023.100914
Received 27 September 2022; Received in revised form 29 December 2022; Accepted 22 January 2023

required to be maintained and processed at room temperature. Thus, this study focuses on supercritical carbon dioxide (SC–CO_2) as the extracting solvent because it has a near ambient critical temperature (31.1 °C), making it a particularly appealing medium for the extraction of biological materials [14]. The key features of SC-CO_2 extraction are its ability in manipulating the dissolving power of CO_2 towards targeted compounds by using appropriate parameters condition. SC-CO_2 extraction also offers the major advantage in term of producing high purity and high selectivity extracts. These have made supercritical fluid technology a primary alternative for the extraction and fractionation of active ingredients compared to traditional solvent extraction such as steam distillation, water extraction, evaporation and spray drying methods that was not sufficient to achieve the exact separation between the desired and the undesired compounds [15].

SC-CO_2 extraction is favoured due to its high selectivity, high efficiency, and short extraction time. Thus, factors influencing the SC-CO_2 extraction process can be adjusted for a dual purpose to improve the extraction efficiency and/or selectivity. Pressure and temperature are predominant during the SC-CO_2 extraction process design and make them influential on both equilibrium and kinetics as well as to control the density and solvating power of CO_2 [16]. The mathematical modelling for SC-CO_2 can be formulated by application of differential equation principle and dimensionless analysis. The process developing mathematical modelling equation is very complex because according to Ref. [17]; in spite of complexity of differential equation, some assumption must be made because most of the equation attempt to analyse data only during steady state conditions. Consequently, since SC-CO_2 extraction phenomena is in unsteady state, the result obtained will affect the simulation of conditions since the solution are approximated in the steady state. For this reason, there will be limitation to the quantitative analysis of SC-CO_2 fluid flow phenomenon. Therefore, the mathematical modelling correlated to the fluid flow phenomena is needed so that better understanding on the parameters that may affect solubility of compounds in SC-CO_2 can be anticipated.

The objective of this study is to determine the solubilization of extract and eugenol in SC-CO_2 from piper bettle leaves. This study also provides the coefficient value of Chrastil and Del Valle Aguilera model fitted the solubility data. The process of solubilization between extract and raw material using SC-CO_2 is determined using the coefficient value of modelling data.

2. Materials and methods

2.1. Pipper Betle leaves preparation

To guarantee that the leaf profiling was equivalent, fresh green *Piper Betle* leaves were procured in bulk from Dedaun Sirih Farm in Selangor, Malaysia. The leaves were washed thoroughly with tap water to remove any dirt and dust present. Then, the leaves were cut using edge tool into small pieces and were oven dried at 40 °C ± 2 °C until no weight change observed. Next, the dried leaves were ground using POLYMIX® PX-MFC 90D, Switzerland (blade grinding assembly) to reduce the particle size for further investigation. To preserve the volatile compound and to maintain the sample freshness, the ground sample were stored in airtight container and kept in freezer (Model Liebherr) at temperature about −30 °C.

2.2. Chemical

The liquid carbon dioxide (99.99% purity) was purchased from Kras Instrument, Johor Bahru, Malaysia. Eugenol standard and methanol HPLC grade was purchased from Sigma-Aldrich (St. Louis, USA).

2.3. Supercritical carbon dioxide (SC–CO_2) extraction

Supercritical fluid extraction was performed using SC-CO_2 extraction system consisting of high-pressure CO_2 piston pump (NS- Tokyo, Japan), 10 mL stainless steel extraction vessel, oven (Venticell, Germany), pressure gauge (Swagelok, USA), chiller (WiseCircu, Korea), heater (WiseCircu, Korea), manual back pressure regulator (Tescom, US), three restrictor valve which are for inlet, outlet and venting operation and CO_2 with 99.99% purity was used as a solvent throughout the process. Supercritical carbon dioxide extraction was performed to extract *Piper Betle* leaves as shown in Fig. 1. The system of SC-CO_2 extraction was dynamic system. The flowrate of CO_2 was measured based on the flowrate of CO_2 pump. The three independent variables involved in this study were pressure (10–30 MPa), temperature (40–80 °C) and flow rate of CO_2 (4–8 mL/min). The constant variables were mean particle size (302.5 μm) and sample moisture content at 8.35% approximately throughout 210 min of extraction time. The system of SC-CO2 extraction was dynamic system.

The equipment system was purged with cotton wool soaked with 3–5 mL of methanol at operating pressure 10 MPa, temperature 40 °C and 4 mL/min of CO_2 flowrate for 10 min (blank extraction) to remove contaminants such as residual oil if any in the system from the extraction process left previously. The limitation of this equipment was pressure cannot above 30 MPa pressureNext, a 5.0 ± 0.005 g of ground dried *Piper betle* leaves that have reached room temperature were loaded into the extraction vessel and before tightly sealed, the vessel was capped with cotton wool to prevent the sample from leaving the extraction vessel. Tubing was connected to the extraction vessel and placed in the oven. Following, oven temperature and CO_2 flowrate were set to the desired operating condition. Liquid CO_2 then were compressed to the desired pressure by controlling the back-pressure regulator. Volume of CO_2 used and extracted oil was recorded every 30 min of the extraction process. Extracts are finally separated from the CO_2 phase and collected in collector at ambient temperature and atmospheric pressure. The CO_2 gas was depressurized to remove from the separator. The extract obtained was sealed and stored at −10 °C to prevent any possible degradation.

2.4. Identification and determination of eugenol using HPLC

The method was developed by Ref. [18] to identify eugenol by High-performance liquid chromatogram (HPLC). The HPLC analysis of extract samples was performed using PerkinElmer Series 200 equip with auto sampler, binary pump, column oven, vacuum degasser and diode array detector. The column used was C_{18} column (5 μm, 4.6 mm ID x 250 mm) with C_{18} guard column. In this study, a 70:30 v/v mixture of methanol and water was chosen as the mobile phase. The elution was performed under isocratic conditions at a flow rate of 0.7 mL/min. Chromatograms were recorded at 280 nm. The oven temperature used was 40 °C.

First, the extract was taken in a 10 mL volumetric flask and were diluted using 7 mL of methanol and 3 mL of distilled water. The solution was vortex for about 30 s, centrifuged for 5 min at 4000 rpm and then sonicated for 10 min. After that, the sample was filtered using nylon membrane filter (0.45 μm) to filter suspended solid and stored in a sample vial for HPLC use. The result was used to study effect of extraction parameters towards eugenol concentration as express in mg of eugenol per grams of extracted *Piper betle* leaves extract at each SC-CO_2 extraction condition and was expressed as follows:

$$\text{Concentration of Eugenol} = \frac{C \times V}{W_{oil}} \tag{1}$$

where, C is concentration of eugenol from analysis (mg/mL), V is volume of the injected solvent in sample (mL) and W_{oil} is weight of extracted *Piper betle* leaves extract in 3.5 h at each extraction condition (mg).

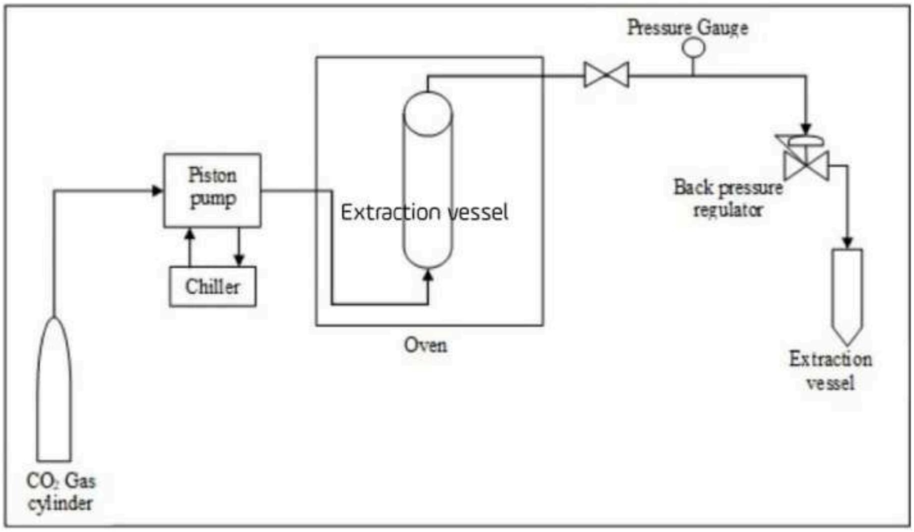


Fig. 1. Schematic diagram for the SC-CO_2 process.

2.5. *Determination of extracted oil yield, g*

Extracted oil can be defined as the accumulation weight of each fraction at given temperature, pressure and flow rate at 210 min of time extraction. The yield was determined by direct weight measurement. The expression of extracted oil as follows:

$$W_{oil} = \sum (W_t - W_b) \tag{2}$$

Where W_{oil} is weight of extracted oil (mg), W_t is weight of oil inside of sample bottle (mg) and $W_{t,f}$ is weight of sample bottle sample (mg).

2.6. *Calculation of solubility of Piper Betle leaves extract in sc-co$_2$*

Solubility was defined as the amount of extracts obtained per mass of fluid used to extract it. In experimental, the solubility was measured by plotting experimental data of mass of oil extracted against the mass of CO_2 used.

$$S\left(\frac{g}{L}\right) = \frac{\Delta y(g)}{\Delta vCO_2(L)} \tag{3}$$

Where $\Delta y(g)$ is the total yield (g); $\Delta V_{CO_2}(L)$ is the total CO_2 consumption (L).

2.7. *Empirical mathematical modelling*

Different equations have been presented for mathematical modelling of solubility data of *Piper Betle* leaves extract in SC-CO_2. The solubility data obtained experimentally were fitted into two density-based semi-empirical models which were Chrastil model [19] and Del Valle and Aguilera model [20]. Multi-linear regression was performed using Excel Solver 2010 to determine the model constants and the best correlation; thus, it was used to present the solubility behaviour of the solid in the SC-CO_2 extraction process. The reliability and accuracy of the models were evaluated using Equation (5). The Chrastil equation can be formed as below:

$$\ln S = k \ln \rho_{CO2} + \frac{a}{T + 273} + b \tag{4}$$

Where S is solubility (g/L), ρ_{CO2} is density of water (g/L) and T is temperature (°C). The value of k depends on average number of solvent molecules in the solvato complex. The value of b depends on the molecular weights of the solute and solvent.

The DVA model was developed using the Chrastil model and the hypothesis that temperature affects the extraction process significantly [21]. The addition of one customizable parameter causes the model's temperature to be more dependent on temperature than density. Eq. (4) shows the Del Valle–Aguilera equation:

$$\ln S = k \ln \rho_{H20} + \frac{a}{T + 273} + \frac{b}{\backslash(T + 273)^2} + c \tag{5}$$

Where S is solubility (g/L), ρ_{H20} is density of water (g/L) and T is temperature (°C). The value of k depends on average number of solvent molecules in the solvato complex and the value of a and b defined as adjustable parameters related to temperature.

2.8. *Average absolute relative deviation (AARD)*

A multilinear regression was performed by using Solver in Excel 2008 program to determine the model constants. The accuracy of Chrastil models and del Valle and Aguilera model were quantified by analysis of average absolute relative deviation (AARD).

$$\text{AARD } (\%) = \frac{1}{n} \sum_{i-1}^{n} \left| \frac{Y_{exp} - y_{caic}}{y_{exp}} \right| \tag{6}$$

where n is number of data points, Y_{exp} is solubility data obtained from experimental respectively at *i*th condition and Y_{calc} is solubility data obtained from Chrastil model respectively at *i*th condition.

3. Results and discussion

Solubility depicts the equilibrium between a solute and a solvent and is a key aspect of separations relating supercritical fluids. Solubility data are valuable process parameters for design and scale up purposes. The solubility value represents the maximum amount of a solute that can be solubilized in a solvent at a given condition. This study conducted mainly to measure the solubility of *Piper Betle* leaves extract in SC-CO_2 and its behaviour at different pressure, temperature and CO_2 flowrate.

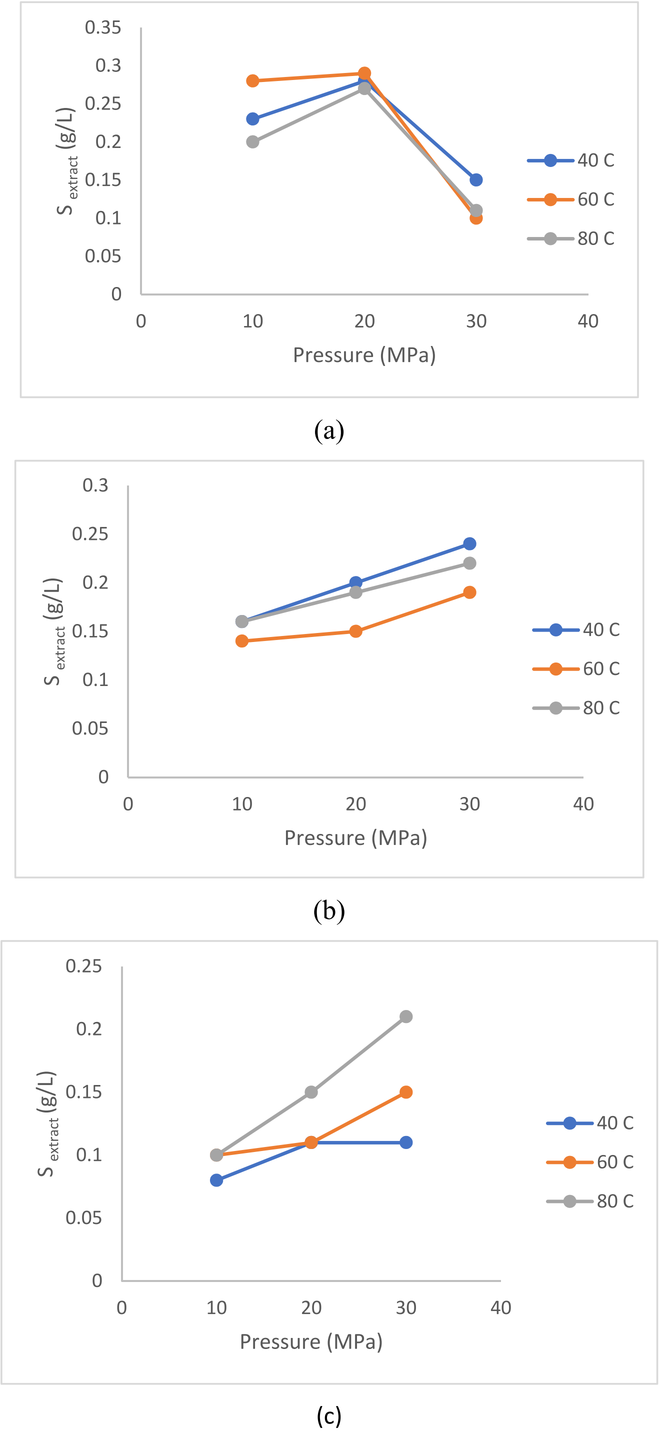
The solubility of *Piper Betle* leaves extract in SC-CO_2 was evaluated at temperatures ranging from 40 °C to 80 °C, pressures ranging from 10 MPa to 30 MPa and CO_2 flow rate ranging from 4 mL/min to 8 mL/min. The solubility data for each condition were obtained from extract divided the volume of carbon dioxide consumption during extraction process curve as shown in equation (2). The experimental solubility data of *Piper Betle* leaves extract in SC-CO_2 and CO_2 density at various operating conditions are presented in Table 1.

3.1. *Effect of SC-CO$_2$ condition on the solubility of Piper Betle leaves extract*

Figs. 2 and 3 show the solubility of *Piper Betle* leaves extract and eugenol in SC-CO$_2$ behaviour at constant flow rate of 4 mL/min, 6 mL/min and 8 mL/min at each constant temperature corresponding to various pressure. As shown in Table 1, it can be observed that the highest solubility of was 0.29 mg/L at the flowrate of 4 mL/min, temperature of 60 °C and pressure of 20 MPa. The highest solubility of eugenol was 9.74E-05 g/L at the highest temperature of 80 °C and lowest pressure of 10 MPa at CO$_2$ flow rate of 4 mL/min. Meanwhile the lowest solubility of extract was 0.08 g/L at the flowrate of 8 mL/min, temperature of 40 °C and pressure of 10 MPa. The lowest solubility of eugenol in SC-CO$_2$ was 2.21E-05 at flowrate of 8 mL/min, temperature of 80 °C and pressure of 30 MPa.

Fig. 2 shows the solubility of *Piper Betle* leaves extract in SC-CO$_2$ at constant flowrate of 4 mL/min, 6 mL/min and 8 mL/min at pressure of 10–30 MPa and temperature of 40–80 °C. Fig. 2(a) shows that pressure of 20 MPa gives the higher solubility of extract compared to 10 and 30 MPa at constant flowrate 4 mL/min. Fig. 2 (a) also illustrates that there is much different in enhancement of temperature from 40 °C to 80 °C . As similar as to Fig. 2(b), the temperature 40 and 80 °C gives the similar solubility of extract. However, Fig. 2(b) and (c) show that the pressure of 30 MPa gives the higher solubility of extract in SC-CO$_2$ at flow rate of 6 mL/min and 8 mL/min. High pressure will increase the density of CO$_2$, thus the solvation power of CO$_2$ also increase [11,22]. The solvation power increase the mass-transfer process between the solute and solvent [23].

Fig. 2(b) and (c) also found that increasing of temperature from 40 °C to 80 °C increase the solubility of extract in SC-CO$_2$. Increasing of temperature increase the vapor pressure of solute to soluble in the SC-CO$_2$ [11,23–25]; Jumakir et al., 2022). Therefore, the extract is easily diluted to the solvent. Decreasing of flowrate from 8 mL/min increase the solubility of *Piper Betle* leaves extract in SC-CO$_2$ as shown in Fig. 2. The higher flowrate will decrease the residence time of solvent/SC-CO$_2$, thus there is not enough contact time of solvent to penetrate and extract the solute [11,14,23,25]; Veza et al., 2022). Furthermore, the higher flow rate will increase the production cost, where high flow rate will consumed higher quantity of CO$_2$ [26]. Therefore, the flowrate of 4 mL/min is suitable to recover of *Piper Betle* leaves extract.



(a)

(b)

(c)

Fig. 2. Solubility of *Piper Betle* leaves extract in SC-CO$_2$ at constant flow rate of 4 mL/min (a), 6 mL/min (b) and 8 mL/min (c).

Table 1
Experimental solubility data of *Piper Betle* leaves extract and eugenol in SC-CO$_2$.

Flowrate (mL/min)	Temperature (°C)	Pressure (MPa)	CO$_2$ Density, (kg/m^3)	Solubility of extract (g/L)	Solubility of eugenol (g/L)
4	40	10	628.62	0.23	7.53E-05
		20	839.82	0.28	7.64E-05
		30	909.89	0.15	6.4E-05
	60	10	289.96	0.28	7.07E-05
		20	723.69	0.29	6.67E-05
		30	829.72	0.10	7.43E-05
	80	10	221.61	0.20	9.74E-05
		20	593.9	0.27	7.77E-05
		30	745.61	0.11	7.4E-05
6	40	10	628.62	0.16	6.01E-05
		20	839.82	0.20	4.83E-05
		30	909.89	0.24	4.1E-05
	60	10	289.96	0.14	6.91E-05
		20	723.69	0.15	5.77E-05
		30	829.72	0.19	5.08E-05
	80	10	221.61	0.16	6.14E-05
		20	593.9	0.19	5.23E-05
		30	745.61	0.22	4.96E-05
8	40	10	628.62	0.08	6.09E-05
		20	839.82	0.11	5.46E-05
		30	909.89	0.11	5.09E-05
	60	10	289.96	0.10	5.5E-05
		20	723.69	0.11	4.93E-05
		30	829.72	0.15	3.61E-05
	80	10	221.61	0.10	5.23E-05
		20	593.9	0.15	3.97E-05
		30	745.61	0.21	2.12E-05

Fig. 2(c) shows that there is cross over pressure occur between temperature of 40 °C and 60 °C. The cross over point is the consequence of competition of two temperature dependent factors which are vapor pressure of the solute and supercritical fluid solvent density [23]. Result obtained from this study shows that at pressure lower the cross over pressure, the density of the solvent become less sensitive to the pressure. This behaviour leads to the increased of solubility as the temperature increases. Commonly, an isobaric increase in temperature results to a decrease in solubility. This phenomenon usually observed in the high compressibility area of the supercritical fluid solvent and it is known as the “retrograde solubility behaviour”. However, density alone does not give the complete explanation of solubility enhancement. Some other factor that responsible for contributing to the solubility behaviour is the volatility of the solid solute [27].

Fig. 3 shows the solubility of eugenol from *Piper Betle* leaves extract to SC-CO_2 at constant flowrate of 4 mL/min (a), 6 mL/min (b) and 8 mL/min (c) at pressure of 10–30 MPa and temperature of 40–80 °C. Fig. 2(a) shows that pressure of 10 MPa gives the higher solubility of extract compared to 10 and 20 MPa at constant flowrate 4 mL/min. Fig. 2 (a) also illustrates that there is much different in enhancement of pressure from 10 to 30 MPa at constant temperature 60 °C. Fig. 2(b) and (c) also show that the pressure of 30 MPa gives the lower solubility of eugenol in SC-CO_2 at flow rate of 6 mL/min and 8 mL/min. High pressure will increase the compactness of *Piper Betle* leaves in the extraction vessel, where the SC-CO_2 cannot penetrate the leaves in the extraction vessel for recovering the eugenol [28,29]. Therefore, the diffusivity of CO2 was decrease with less contact area between the solute and solvent [30] (see Fig. 4).

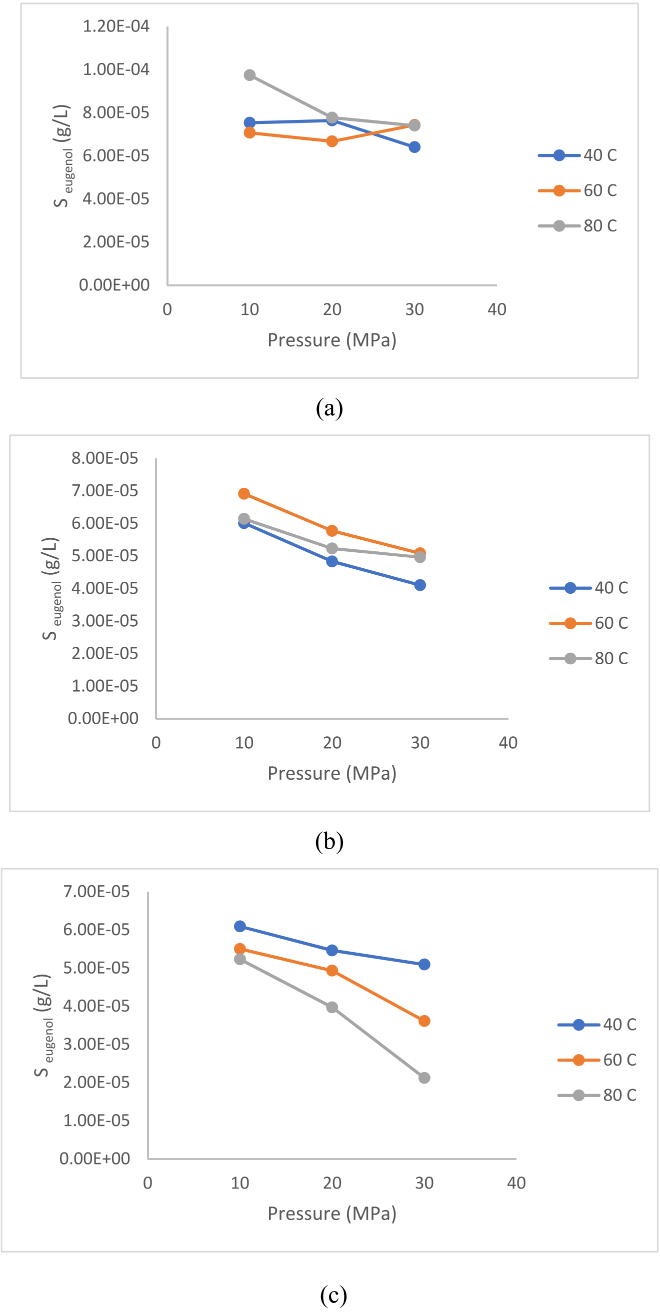


Fig. 3. Solubility of eugenol from *Piper Betle* leaves to SC-CO_2 at constant flow rate of 4 mL/min (a), 6 mL/min (b) and 8 mL/min (c).

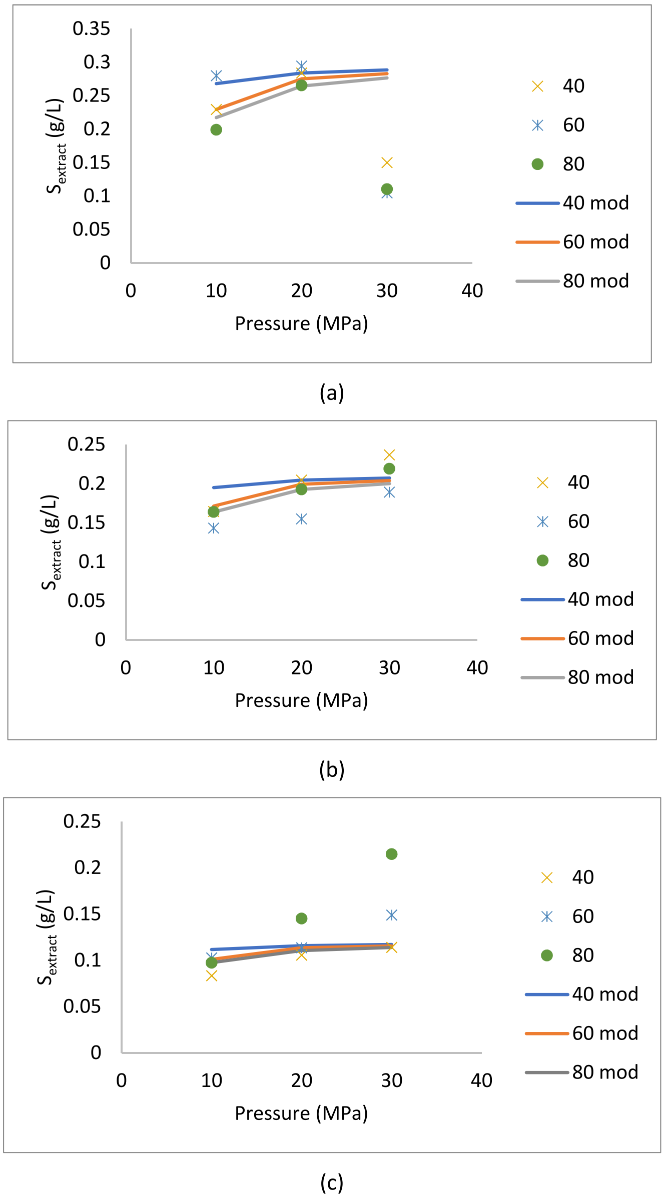


Fig. 4. Solubility of *Piper Betle* leaves extract to SC-CO_2 fitted by Chrastil model at constant flowrate 4 mL/min (a), 6 mL/min (b) and 8 mL/min (c).

Fig. 2(a) also found that increasing of temperature from 40 °C to 80 °C increase the solubility of eugenol in SC-CO_2. Increasing of temperature increase the vapor pressure of eugenol to soluble in the SC-CO_2 [31]. However, temperature of 40 °C gives the higher solubility of eugenol in SC-CO_2 as shown in Fig. 3(c). Lower temperature condition will increase the density of CO_2, where higher density will increase the diffusivity and solvation power of solvent [32]. Therefore, the extract is easily diluted to the solvent due to high mass-transfer process between solute and solvent. The flowrate from 6 mL/min gives higher the solubility of eugenol from *Piper Betle* leaves in SC-CO_2 as shown in Fig. 3. The higher flowrate will decrease the residence time of solvent/SC-CO_2, thus there is not enough contact time of solvent to penetrate and extract the solute. Furthermore, the higher flow rate will increase the production cost, where high flow rate will consumed higher quantity of CO_2 [33]. Therefore, the flowrate of 6 mL/min is suitable to recover of eugenol from *Piper Betle* leaves.

Fig. 2(c) shows that there is cross over pressure occur between temperature of 40 °C and 60 °C. The cross over point is the consequence of competition of two temperature dependent factors which are vapor pressure of the solute and supercritical fluid solvent density [23]. Result obtained from this study shows that at pressure lower the cross over pressure, the density of the solvent become less sensitive to the pressure. This behaviour leads to the increased of solubility as the temperature increases. Commonly, an isobaric increase in temperature results to a decrease in solubility. This phenomenon usually observed in the high compressibility area of the supercritical fluid solvent and it is known as the "retrograde solubility behaviour". However, density alone does not give the complete explanation of solubility enhancement. Some other factor that responsible for contributing to the solubility behaviour is the volatility of the solid solute [27].

From the observation, at constant flow rate of 4 mL/min as shown in Fig. 3(a), there was a convergence of the solubility isotherm curve. The interaction points of the solubility isotherms termed as cross over pressure. At the lowest flow rate, the crossover was in between 20 MPa and 30 MPa. Meanwhile, at flow rate of 6 mL/min, it was observed that the crossover was at 30 MPa on 60 °Cand 80 °C. However, at constant flow rate of 6 and 8 mL/min (Fig. 3(b)), there is no cross over pressure occur. The cross over point is the consequence of competition of two temperature dependent factors which are vapor pressure of the solute and supercritical fluid solvent density [25].

As a matter of fact, the retrograde solubility behaviour is explained by the relative influence of the density effect and the volatility effect. An isobaric increase in temperature decreases density of the supercritical fluid solvent and hence decreases the solubility by the density effect [34]. On the other hand, the same increase in temperature increases the volatility of the solute and hence increases the solubility by the volatility effect. At a pressure less than the crossover pressure, the volatility effect is more pronounced than the density effect, facilitating an increase in solubility with an increase in temperature [35].

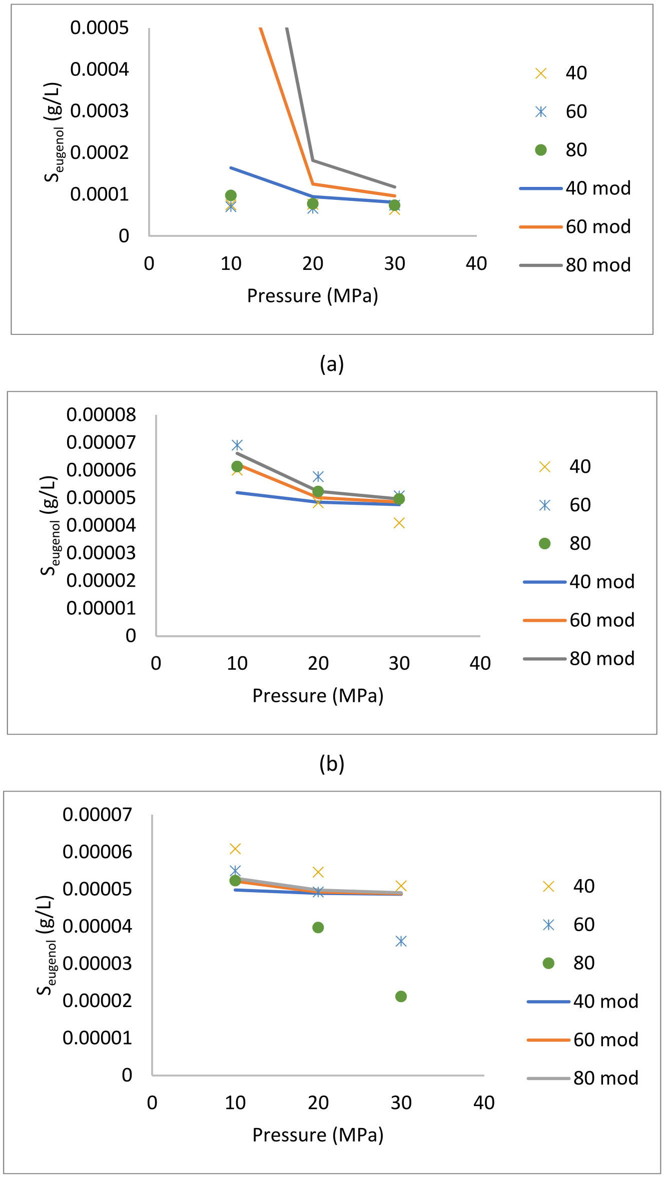
3.2. *Empirical modelling*

The solubility data in SFE technology can be conveniently correlated in terms of density rather than pressure or temperature. In fact, the density of the solvent is closely related to those two operating conditions. Therefore, two semiempirical density-based equations (Chrastil and del Valle and Aguilera) were attempted to correlate the solubility of *Piper Betle* leaves extract and eugenol, respectively in $SC\text{-}CO_2$ system.

3.2.1. *Chrastil model*

To study the solubility of extract in supercritical fluid, Chrastil model is used to fit the model with the experimental data by plotting the graph of solubility versus density of fluid. Figs. 5 and 6 show the graphical correlation between experimental data and Chrastil equation at constant flow rate of 4, 6 and 8 mL/min. In addition, Table 2 shows the of estimated parameters and AARD % for the supercritical fluid extraction system obtained by Chrastil.

In Chrastil's equation, the parameters obtained represent important term. For parameter a, it represents the heat of solvation and vaporization of the solute, meanwhile parameter b represents the molecular weight and melting point of solute involved and k represents the average number of molecules that form the solvate-complex. From the analysis of the results, the average AARD% of correlation between the solubility experimental data with the Chrastil's equation obtained was 6.71%. The lowest AARD% of correlation between the solubility of *Piper Betle* leaves extract in $SC\text{-}CO_2$ with the Chrastil's equation obtained was 8.03% at constant flowrate 6 mL/min. The lowest AARD% of correlation between the solubility of eugenol in $SC\text{-}CO_2$ with the Chrastil's equation obtained was 0.79% at constant flowrate 6 mL/min. Additionally, according to Khimeche et al. (2007) the coefficient value of a is related to temperature effects where it shows whether the extraction is exothermic or endothermic reaction to increase or decrease the solubility extract. Negative value of coefficient represents the endothermic reaction and positive value of a represents exothermic reaction. Meanwhile, the coefficient value of b depends on the molecular weights of the solute and solvent.



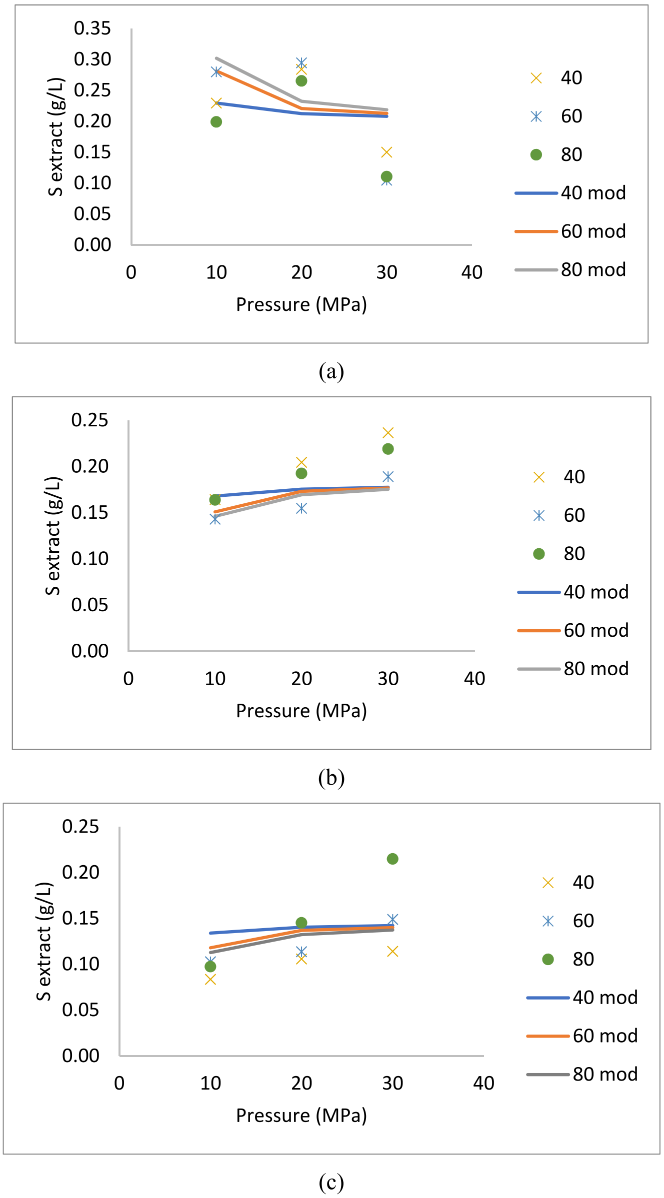
(a)

(b)

(c)

Fig. 5. Solubility of eugenol from *Piper Betle* leaves in $SC\text{-}CO_2$ fitted by Chrastil model at constant flowrate 4 mL/min (a), 6 mL/min (b) and 8 mL/min (c).

By referring Table 2, it shows that as the flow rate increase the value of a change from exothermic reaction to endothermic reaction. This indicate that the increasing in the solvent flow rate will increase the convection effects on the extraction process, lowering the mass transfer resistance and increase the intermolecular interaction between the solvent and solute at the same time [36,37]. This occurrence was corresponding with the value of k which represent the average number of molecules that form the solvate-complex where the result show that the k value decreased as the CO_2 flow rate increased. This result obtained as



(a)

(b)

(c)

Fig. 6. Solubility of *Piper Betle* leaves extract to SC-CO_2 fitted by Del Valle and Aguilera (DVA) model at constant flowrate 4 mL/min (a), 6 mL/min (b) and 8 mL/min (c).

Table 2
Correlation data of *Piper Betle* leaves extract and eugenol solubility in SC-CO_2 fitted by Chrastil model at constant flowrate 4 mL/min, 6 mL/min and 8 mL/min.

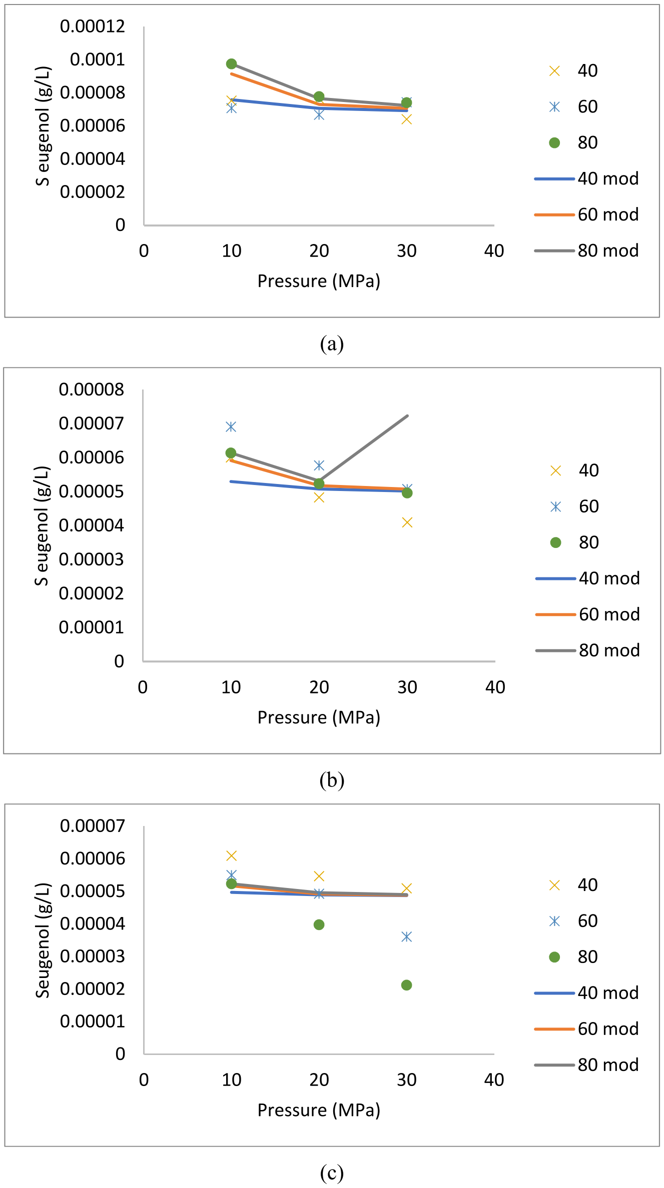
Compound	Flow rate (mL/min)	k	a	b	AARD (%)
Piper Betle leaves extract	4	0.2	7.48	−2.62	17.5
	6	0.17	7.47	2.72	5.77
	8	0.13	7.47	−3.04	9.64
Eugenol	4	−1.90	13.21	3.46	9.64
	6	−0.24	12.90	−8.38	0.79
	8	−0.06	13.16	−9.54	1.92
Average					6.71

parallel with the effect of solubility of *Piper Betle* leaves extract in SC-CO_2 discussed in section 3.1 where the solubility of extracted oil decreased as the CO_2 flow rate increased. According to Mohd, (2016), the increasing value of k indicates the number of solvents interact with the solute increases.

3.2.2. Del Valle and Aguilera model

Del Valle and Aguilera (DVA) model were an extension of Chrastil equation with additional temperature dependant parameter added to the model [20]. Likewise, to Chrastil equation, logarithmic function of solubility was plotted against logarithmic function of density of fluid. The adjustable parameter was independent to the influence of solvent flow rate. Due to this reason, the values of adjustable parameters were not the same for all flow rates. Figs. 7 and 8 show the graphical correlation between DVA model and the solubility of *Piper Betle* leaves extract in SC-CO_2 at constant flow rate of 4, 6 and 8 mL/min. Table 3 also shows the adjustable parameters value as a function to the DVA model.

In del Valle and Aguilera equation, the parameters used were the same as Chrastil's equation and *c* was the additional constant for the model and the additional temperature term that has been modified by taking into consideration the variation of heat of vaporization of the solute [20]. From the analysis of the results, the average AARD (%) of correlation between the solubility experimental data with the DVA's



(a)

(b)

(c)

Fig. 7. Solubility of eugenol to SC-CO_2 fitted by Del Valle and Aguilera (DVA) model at constant flowrate 4 mL/min (a), 6 mL/min (b) and 8 mL/min (c).

Table 3
Correlation data of *Piper Betle* leaves extract and eugenol solubility in SC-CO_2 fitted by DVA model at constant flowrate 4 mL/min, 6 mL/min and 8 mL/min.

Compound	Flow rate (mL/min)	k	a	b	c	AARD (%)
Piper betle leaves extract	4	−0.27	8.02	2.62	0.22	18.6
	6	0.15	−47.95	2.61	2.61	8.03
	8	0.16	6.99	−3.04	−3.06	11.11
eugenol	4	−0.25	12.95	3.46	−7.95	18.05
	6	−0.15	13.02	3.46	−8.95	1.17
	8	−0.05	13.91	−9.54	−9.60	1.91
Average						6.21

equation obtained was 6.2%. The lowest AARD% of correlation between the solubility of *Piper Betle* leaves extract in SC-CO_2 with the DVA's equation obtained was 8.03% at constant flowrate 6 mL/min. The lowest AARD% of correlation between the solubility of eugenol in SC-CO_2 with the DVA's equation obtained was 1.17% at constant flowrate 6 mL/min. By referring Table 3, it shows that the value of k which represent the average number of molecules that form the solvate-complex increased as the CO_2 flow rate increased. This shows a good agreement of DVA equation to the solubility of *Piper Betle* leaves extract in SC-CO_2 as a function of density to the extraction process whereas the CO_2 flow rate increased the solubility increased. From the result of constants value obtained from Charstil and Del Valle and Aguilera equation, it can be concluded that flow rate also play an important role along with pressure and temperature to maximum the amount of a solute that can be solubilized in a solvent.

4. Conclusion

Piper Betle leaves, which contain a high concentration of eugenol, are widely cultivated and transported across several Asian nations. Eugenol is an essential primary phytochemical present in betel leaves. The variables were 10 MPa–30 MPa of pressure, 40 °C–60 °C of temperature, and 4 mL/min to 8 mL/min of flow rate. In the solubility investigation, the Chrastil model correlated the solubility data of *Piper Betle* leaves extract with the lowest average absolute relative deviation (AARD), which was 6.20%. At flow rates of 4, 6, and 8 mL/min, the coefficient values of k for extract solubility were −0.27, 0.17, and 0.16, respectively. In addition, the values of k for eugenol solubility at flow rates of 4, 6, and 8 mL/min were −0.25, −0.15, and −0.05, respectively. To boost the solubility of Piper beetle extract and eugenol, it is hypothesized that the solvation power of SC-CO_2 was stronger at slow flow rates. From its application point of view, governing by the needs to enhance the extraction efficiency, the comprehensive design of Supercritical CO_2 extraction process and its fundamental of mechanism in the process to access high quality and quantity of valuable compounds in *Piper Betle* leaves. This will be useful in scaling up of industrial SFE processes.

Funding declaration

This work was supported by Faculty of Food Science and Nutrition, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia and UTM Post-Doctoral Scheme (R.J130000.7113.05E53).

Author contribution

Nur Husnina Arsad: Conceptualization and writing original draft, Nicky Rahmana Putra: Visualization, Investigation, Nur Salsabila Md Norodin: Writing- Reviewing and Editing, Ahmad Hazim Abdul Aziz: Writing- Reviewing and Editing, Zuhaili Idham: Writing- Reviewing and Editing, Mohd Azizi Che Yunus: Supervision.

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.

Data availability

Data will be made available on request.

Acknowledgement

The authors would like to acknowledge the Faculty of Food Science and Nutrition, Universiti Malaysia Sabah, Kota Kinabalu, Sabah, Malaysia for the publication fee given and Professional Development Research University grant (R.J130000.7113.05E53) from Universiti Teknologi Malaysia for supporting this work.

References

[1] F. Jamshidi-Kia, Z. Lorigooini, H. Amini-Khoei, Medicinal plants: past history and future perspective, J. Herbmed Pharmacol. 7 (1) (2018).

[2] I. Ali, F.G. Khan, K.A. Suri, B.D. Gupta, N.K. Satti, P. Dutt, I.A. Khan, In vitro antifungal activity of hydroxychavicol isolated from Piper betle L, Ann. Clin. Microbiol. Antimicrob. 9 (1) (2010) 1–9.

[3] D. Chakraborty, B. Shah, Antimicrobial, antioxidative and antihemolytic activity of Piper betel leaf extracts, Int. J. Pharm. Pharmaceut. Sci. 3 (3) (2011) 192–199.

[4] P. Valentão, R.F. Gonçalves, C. Belo, P.G. de Pinho, P.B. Andrade, F. Ferreres, Improving the knowledge on Piper betle: targeted metabolite analysis and effect on acetylcholinesterase, J. Separ. Sci. 33 (20) (2010) 3168–3176.

[5] R.R. Lubis, D.D.W. Marlisa, Antibacterial activity of betle leaf (Piper betle l.) extract on inhibiting Staphylococcus aureus in conjunctivitis patient, Am. J. Clin. Experiment. Immunol. 9 (1) (2020) 1.

[6] F. Fadilah, A. Yanuar, A. Arsianti, R. Andrajati, Phenylpropanoids, eugenol scaffold, and its derivatives as anticancer, Asian J. Pharmaceut. Clin. Res. (2017) 41–46.

[7] N.H. Arsad, M.A.C. Yunus, Z. Idham, Optimization and effect of supercritical carbon dioxide extraction conditions on global oil yield and eugenol from piper betle leaves, Mal. J. Fund. Appl. Sci 13 (4) (2017) 680–684.

[8] G.P. Kamatou, I. Vermaak, A.M. Viljoen, Eugenol—from the remote Maluku Islands to the international market place: a review of a remarkable and versatile molecule, Molecules 17 (6) (2012) 6953–6981.

[9] T. Hintz, K.K. Matthews, R. Di, The Use of Plant Antimicrobial Compounds for Food Preservation, BioMed research international, 2015, 2015.

[10] O.A. Odunlami, D.A. Vershima, T.E. Oladimeji, S. Nkongho, S.K. Ogunlade, B. S. Fakinle, Advanced techniques for the capturing and separation of CO2 – a review, Results in Engineering 15 (2022), 100512, https://doi.org/10.1016/j.rineng.2022.100512.

[11] D.N. Rizkiyah, W.M.S.W. Jusoh, Z. Idham, N.R. Putra, M.A. Che Yunus, Investigation of phenolic, flavonoid and antioxidant recovery and solubility from roselle using supercritical carbon dioxide: experimental and modelling, J. Food Process. Preserv. (2022), e16670.

[12] N.F.M. Idrus, L.N. Yian, Z. Idham, N.A. Aris, N.R. Putra, A.H.A. Aziz, M.A.C. Yunus, Mini review: application of supercritical carbon dioxide in extraction of propolis extract, J. Malays. J. Fundam. Appl. Sci 14 (2018) 387–396.

[13] W. Mens-Appamana, J. Yencham, S. Putivisutisak, P. Bumphenkiattikul, A. Vongachariya, W. Khaodee, S. Assabumrungrat, Investigation of mass transfer and hydrodynamics of liquid-liquid extraction in spinning disc reactor by computational fluid dynamics simulation, Results in Engineering 16 (2022), 100798, https://doi.org/10.1016/j.rineng.2022.100798.

[14] H. Mohd-Nasir, N.R. Putra, S.C. Chuo, N.M. Daud, H. Hartati, N. Bakeri, L. Md Salleh, Optimization of the supercritical carbon dioxide extraction of Quercus infectoria galls extracts and its bioactivities, J. Food Process. Preserv. 45 (2) (2021), e15156.

[15] A. Aziz, M. Yunus, N. Arsad, N. Lee, Z. Idham, A. Razak, Optimization of supercritical carbon dioxide extraction of Piper Betel Linn leaves oil and total phenolic content, IOP Conf. Ser. Mater. Sci. Eng, in: Paper presented at the2nd International Conference on Chemical Engineering (ICCE) Universitas Parahiyangan, 26–27 October 2016, Bandung, Indonesia, 2016.

[16] P.A. Uwineza, A. Waśkiewicz, Recent advances in supercritical fluid extraction of natural bioactive compounds from natural plant materials, Molecules 25 (17) (2020) 3847.

[17] E. Alonso, F. Cantero, J. Garcıa, M. Cocero, Scale-up for a process of supercritical extraction with adsorption of solute onto active carbon. Application to soil remediation, J. Supercrit. Fluids 24 (2) (2002) 123–135.

[18] N. Singtongratana, S. Vadhanasin, J. Singkhonrat, Hydroxychavicol and eugenol pro ling of betel leaves from piper betle L. Obtained by liquid-liquid extraction and supercritical fluid extraction, Agriculture and Natural Resources 47 (4) (2013) 614–623.

[19] J. Chrastil, Solubility of solids and liquids in supercritical gases, J. Phys. Chem. 86 (15) (1982) 3016–3021.

[20] J.M. Del Valle, J.M. Aguilera, An improved equation for predicting the solubility of vegetable oils in supercritical carbon dioxide, Ind. Eng. Chem. Res. 27 (8) (1988) 1551–1553.

[21] D. Valle, Aguilera, An improved equation for predicting the solubility of vegetable oils in supercritical carbon dioxide, Ind. Eng. Chem. Res. 27 (8) (1988) 1551–1553.

[22] A.H. Abdul Aziz, N.R. Putra, H. Kong, M.A. Che Yunus, Supercritical carbon dioxide extraction of sinensetin, isosinensetin, and rosmarinic acid from Orthosiphon stamineus leaves: optimization and modeling, Arabian J. Sci. Eng. 45 (9) (2020) 7467–7476.

[23] Z. Idham, N.R. Putra, H. Nasir, L.N. Yian, N.F.M. Idrus, M.A.C. Yunus, Extraction and solubility modeling of anthocyanins rich extract from Hibiscus sabdariffa L. Using supercritical carbon dioxide, Malaysian Journal of Fundamental and Applied Sciences 17 (6) (2021) 720–730.

[24] A.H. Abdul Aziz, N.F. Mohd Idrus, N.R. Putra, M.A. Awang, Z. Idham, H. Mamat, M.A. Che Yunus, Solubility of rosmarinic acid in supercritical carbon dioxide extraction from orthosiphon stamineus leaves, ChemEngineering 6 (4) (2022) 59.

[25] N.R. Putra, D.N. Rizkiyah, A.S. Zaini, S. Machmudah, M.A.C. Yunus, Solubility of catechin and epicatechin from Arachis Hypogea skins wastes by using supercritical carbon dioxide-ethanol and its optimization, J. Food Meas. Char. 15 (2) (2021) 2031–2038.

[26] T. Arumugham, R. K, S.W. Hasan, P.L. Show, J. Rinklebe, F. Banat, Supercritical carbon dioxide extraction of plant phytochemicals for biological and environmental applications – a review, Chemosphere 271 (2021), 129525, https://doi.org/10.1016/j.chemosphere.2020.129525.

[27] A.H. Abdul Aziz, N.R. Putra, A.S. Zaini, Z. Idham, M.Z. Ahmad, M.A. Che Yunus, Solubility of sinensetin and isosinensetin from Cat's Whiskers (Orthosiphon stamineus) leaves in ethanol-assisted supercritical carbon dioxide extraction: experimental and modeling, Chem. Pap. 75 (12) (2021) 6557–6563.

[28] N.M. Daud, N.R. Putra, R. Jamaludin, N.S.M. Norodin, N.S. Sarkawi, M.H. S. Hamzah, L.M. Salleh, Valorisation of plant seed as natural bioactive compounds by various extraction methods: a review, Trends Food Sci. Technol. 119 (2022) 201–214.

[29] L.N. Yiana, N.R. Putraa, Z. Idhama, N.F. Mohd, A.H.A.A. Idrusa, S.H.M. Setaparb, C. Yunusa, Supercritical carbon dioxide extraction of hevea brasiliensis seeds: influence of particle size on to oil seed recovery and its kinetic, Malaysian Journal of Fundamental and Applied Sciences 17 (3) (2021) 253–261.

[30] N.R. Putra, A.H.A. Aziz, Z. Idham, M.S.H. Ruslan, M.A.C. Yunus, Diffusivity optimization of supercritical carbon dioxide extraction with co-solvent-ethanol from peanut skin, Malaysian Journal of Fundamental and Applied Sciences 14 (1) (2018) 9–14.

[31] S. Zabihi, S.H. Esmaeili-Faraj, F. Borousan, A.Z. Hezave, S. Shirazian, Loxoprofen solubility in supercritical carbon dioxide: experimental and modeling approaches, J. Chem. Eng. Data 65 (9) (2020) 4613–4620.

[32] M.S. De Oliveira, S.G. Silva, J.N. da Cruz, E. Ortiz, W.A. da Costa, F.W.F. Bezerra, E. de Aguiar Andrade, Supercritical CO2 application in essential oil extraction, Industrial Applications of Green Solvents 2 (2019) 1–28.

[33] C. Espinosa Álvarez, R. Vardanega, F. Salinas-Fuentes, J. Palma Ramírez, W. Bugueño Muñoz, D. Jiménez-Rondón, M.C. Ruiz-Domínguez, Effect of CO2 flow rate on the extraction of astaxanthin and fatty acids from Haematococcus pluvialis using supercritical fluid technology, Molecules 25 (24) (2020) 6044.

[34] C.J. Cockrell, O. Dicks, L. Wang, K. Trachenko, A.K. Soper, V.V. Brazhkin, S. Marinakis, Experimental and modeling evidence for structural crossover in supercritical CO 2, Phys. Rev. 101 (5) (2020), 052109.

[35] M. Pishnamazi, S. Zabihi, P. Sarafzadeh, F. Borousan, A. Marjani, R. Pelalak, S. Shirazian, Using static method to measure tolmetin solubility at different pressures and temperatures in supercritical carbon dioxide, Sci. Rep. 10 (1) (2020) 1–7.

[36] N.R. Putra, D.N. Rizkiyah, Z. Idham, J. Jumakir, W. Waluyo, A.N. Mohd Faizal, M. A. Che Yunus, A New solubility model for competing effects of three solvents: water, ethanol, and supercritical carbon dioxide, Separ. Sci. Technol. (2022) 1–7.

[37] N.R. Putra, D.N. Rizkiyah, Z. Idham, I. Veza, L. Qomariyah, M.A.C. Yunus, Optimization and modelling in flavonoid and phenolic compounds recovery from peanut skin by subcritical water, Biomass Conversion and Biorefinery (2022) 1–11.