RESEARCH ARTICLE

Kinetic modelling and extraction of *Orthosiphon stamineus* stems and leaves by SC-CO₂

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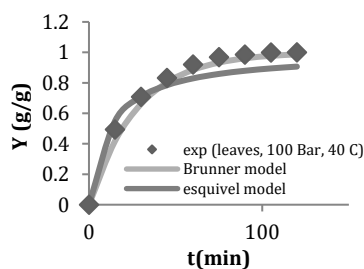* Corresponding author: azizi@cheme.utm.my and rahmana@utm.my

Graphical abstract

Abstract

The aims of this study are to determine the effect of parameters on the extraction yield of *Orthosiphon stamineus* stems and leaves extract and to examine the mass transfer process by kinetic models to obtain the extraction rate of supercritical carbon dioxide. Other objective is to compare the antioxidant activity of *Orthosiphon stamineus* stems and leaves extract using supercritical carbon dioxide extraction and Soxhlet extraction. Extraction parameters involved were pressure (10 and 30 MPa) and temperature (40 and 80 °C). DPPH method was used to examine the antioxidant activity of extract. A better correlation of kinetic mass transfer data has successfully fitted using Brunner model compared with Esquivel model with 6.09% average AARD and 0.992 coefficient of determination. The extraction rate of *Orthosiphon stamineus* leaves and stems were found to be in the rage of 0.52×10^{-3} to 8.84×10^{-3} g/min and $0.8160.52 \times 10^{-3}$ to 8.816×10^{-3} g/min, respectively. The maximum antioxidant activity of *Orthosiphon stamineus* stems and leaves extract were 91.58% and 88%. Similarity in the quality for both extract of *Orthosiphon stamineus* stems and leaves makes the separation to be unnecessary.

Keywords: *Orthosiphon stamineus*; supercritical carbon dioxide; extraction rate; antioxidant activity; modelling

INTRODUCTION

One of the well-known medicinal herbs in Malaysia, *Orthosiphon stamineus* is believed to be originated from Southeast Asian countries such as Malaysia, Thailand, Indonesia, Philippines, and Brunei. Due to high antioxidant activity and rich in bioactive compounds in *Orthosiphon stamineus*, this plant has been identified as one of the potential and high valuable herbs [1]. Moreover, *Orthosiphon stamineus* is used traditionally as a medicine to treat several diseases such as diabetes, hypertension, kidney problem, bladder inflammation, gout, and diabetes [2]. In the herbs manufacturing, *Orthosiphon stamineus* stems are zero-value materials and are commonly separated from leaves; but in this research, the antioxidant activity of *Orthosiphon stamineus* stems is evaluated in order to compare with the antioxidant activity of its leaves.

Soxhlet extraction as an established conventional method is usually used to extract *Orthosiphon stamineus* with high quantity of extract, but extract produced is of poor quality. Supercritical carbon dioxide extraction, on the other hand, is an established modern technology used to extract plants and herbs with high quality of extract. The advantages of using supercritical carbon dioxide (SC-CO₂) include high purity of extract that is free from organic solvent and solute content. Significantly, by using this approach, high amount of bioactive compound in the extract can be achieved. Since SC-CO₂ has low critical temperature and pressure, bioactive compound is not easily degraded. Moreover, the solubility of supercritical carbon dioxide as solvent can be manipulated to get maximum yield and selected compound [3, 4]. High diffusivity of solvent gives supercritical carbon dioxide ability to carry out higher bioactive compound compared with conventional extraction method [5].

SC-CO₂ extraction have been used by many researchers to obtain bioactive compounds from plants and herbs effectively, such as extraction of total phenolic compound from *Piper betel* Linn leaves oil [6], lycopene extraction from tomato skin [7], extraction of peanut skin oil [8-10], and extraction *Pithecellobium jiringa* seeds to obtain djenkolic acid [11], palm-pressed fiber [12].

Determination and analysis of antioxidant activity of the extract is usually done using 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH) method because of its rapid and accurate results [13, 14]. Previous researches showed that DPPH method has successfully examined the hard wheat extract [15], peanut skin oil [16], pistachio oil [17], grape seeds oil[18], *Artocarpus heterophyllus L.* oil, [14] and tomato extract [13].

To date, studies about mass transfer studies of *Orthosiphon stamineus* extraction by supercritical carbon dioxide are unavailable. Studies on mass transfer are important because it can help to enhance and encourage the extraction process in order to obtain high quantity and quality extract. One of the mass transfer parameters is extraction rate. The Esquivel and Brunner models have been used to calculate the extraction rate of extraction process [8]. The Esquivel and Brunner models are the first order models that have one adjustable parameter. Therefore, the models can be easily used to determine the extraction process [19].

This study was conducted to determine the effect of parameters on the extraction of *Orthosiphon stamineus* stems and leaves to obtain high yield extract and antioxidant activity. The second objective was to

correlate the extraction oil yield of *Orthosiphon stamineus* stems and leaves extracts by kinetic models to obtain extraction rate of experimental data. The other objective was to compare the antioxidant activity of supercritical carbon dioxide extraction and Soxhlet extraction on the extraction of *Orthosiphon stamineus* stems and leaves.

EXPERIMENTAL

Materials and sample preparation

The sun-dried *Orthosiphon stamineus* plant was obtained from Bioalpha Sdn. Bhd. Before being ground, the leaves and stems of the dried plant was separated. Then, they were powdered using dry-mill grinder with the aim of increasing the samples' surface area. In order to obtain the same particle size, the dried powdered leaves and stems were sieved by using sieve trays (355 to 425 µm). The powdered samples were kept in a sealed plastic bag and stored at −20 °C to maintain the freshness before being used for extraction [20]. Liquid carbon dioxide (99% purity) was purchased from Kras Instrument, Johor Bahru, Malaysia. Technical grade of ethanol (99.86%) was obtained from Merck, USA.

Experimental procedure

The semi-batch process was used on the SC-CO$_2$ extraction with continuous counter current flow as shown in Fig. 1 and 2. The ratio of modifier ethanol was 5%V/V$_{CO2}$ to enhance the polarity of solvent to extract polar compounds.

The chiller and heater temperature were set at 5 °C and 50 °C, respectively. A total of 15 grams samples was inserted put into the extraction vessel. The parameters are pressure (100 and 300 bar) and temperature (40 and 80 °C) with 2 hours extraction time and the constant flow rate of CO$_2$ was 10 g/min. The extract was collected for every 15 minutes. The schematic of the process is shown in Fig. 2. The extract obtained were placed in the collection vials, sealed and stored in a chiller at 2.7 °C to prevent any possible degradation of the product.

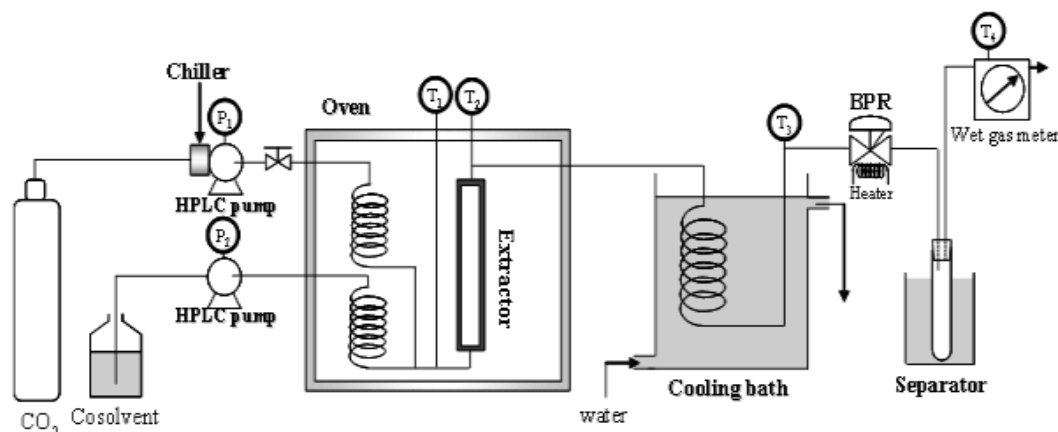**Fig. 1.** Supercritical fluid extraction unit.

Fig. 2. The schematic diagram of SFE unit.

Soxhlet extraction as a conventional method

Food grade ethanol 99.86 % (Merck, USA.) was used to extract *Orthosiphon stamineus* leaves and stems. 100 mL of solvent was added into the Soxhlet apparatus. Thimble containing 5.0 ± 0.005 g of *Orthosiphon stamineus* powder was placed in the Soxhlet apparatus. The Soxhlet extraction time was 6 hours with temperature based on the boiling point of ethanol which is 78 °C. Furthermore, the extract was separated by a vacuum dry. The pressure and temperature of vacuum dry was at 80 mBar and 40 °C, respectively.

Analysis of global yield

The global yield was calculated using the following Equation (1):

Extract Yield (g/g) $= \frac{m_a}{m_{ab}}$ (1)

where m$_a$ is mass of the extract in gram and m$_{ab}$ is mass of sample in gram.

Mass Transfer by Kinetic Models

The extraction data graphs for 8 experimental runs were fitted to the kinetic models to obtain the extraction rate. The mass transfer models, Esquivel and Brunner, are the first order models that have one

adjustable model which makes it easily fitted between experimental data and models. Due to the one adjustable model, the error between models and experimental data can be minimalized [21]. The Esquivel model is presented in the Equation (2):

$$\frac{Y_t}{Y_2} = \left(\frac{t}{k_2 + t} \right) \qquad (2)$$

where Y_t is the actual mass of extract yield (g), Y_2 is the predicted total mass of extract yield by model (g), t is represent time at each fraction (sec), and k_2 is the adjustable parameters (sec). The Brunner equation represents the empirical model and a specific solution of Fick's law [22]:

$$\frac{Y_t}{Y_2} = (1 - e^{-k_1 t}) \qquad (3)$$

where $\frac{Y_t}{Y_2}$ (g/g) is the extraction yield divided by the predicted total mass of extract yield, Y_2 by model (g), k is the rate constant (min^{-1}), t is the extraction time (sec). This equation has one adjustable parameter (k_1) [19].

Average absolute relative deviation percentage (AARD%)

Determination of suitable model that is correlated with the experimental data, the average absolute relative deviation percentage

(AARD%) between model and experimental was used. The equation is as follows:

$$AARD\% = \frac{1}{n} \sum_{i=1}^{n} \left| \frac{\ln Y_{model} - \ln Y_{exp}}{\ln S_{exp}} \right| \quad (4)$$

where n is the number of data points, Y_{exp} is the experimental yield obtained and Y_{model} is the calculated yield using the model. Furthermore, coefficient of determination was used to give information about the goodness of model that fitted the experimental data. $R^2 > 0.8$ indicates that the model fits the experimental data successfully. The equation of coefficient for determination, R^2 is shown as Equation (4)

$$R^2 = 1 - \frac{\sum_i (y_i - f_i)^2}{\sum_i (y_i - \bar{y})^2} \quad (5)$$

where $\sum_i (y_i - f_i)^2$ the residual data as error of model is correlated the experimental data and $\sum_i (y_i - \bar{y})^2$ is the variance of the data.

2,2-Diphenyl-1-Picryl-Hydrazyl-Hydrate (DPPH) method for analysis of antioxidant activity

The antioxidant activity of *Orthosiphon stamineus* leaves and stems extract were evaluated as described by previous study [23, 24]. First, 0.5 µg/L of *Orthosiphon stamineus* leaves and stems extracts were mixed with 0.165 mM ethanoic 2,2-diphenyl-1-picryl-hydrazyl-hydrate (DPPH). The incubation time of sample at room temperature was 30 min, the optimum absorbance spectrophotometer UV-Vis was at 516 nm and converted into percentage of antioxidant activity (% AA). The calculation of antioxidant activity was made using the following equation:

$$(\% \ AA) = \frac{(A_y - A_x)}{A_x} \ x \ 100\% \quad (6)$$

where %AA is percentage of antioxidant activity, A_y is absorbance of DPPH solutions before addition of sample, and A_x is absorbance of mixture between DPPH solutions with addition extract solution.

RESULTS AND DISCUSSION

Pressure and temperature were the main variables in order to determine high extract and extraction rate. Thus, by knowing the effect of both variables on the extraction using SC-CO_2, the yield of extraction can be enhanced. The pressure (100 and 300 bar) and temperature (40 and 80 °C) were chosen. Based on the preliminary results, constant parameters for extraction of *Orthosiphon stamineus* by supercritical carbon dioxide were 5% ratio of co-solvent ethanol with 300 µm particle size of samples. In order to determine the extraction rate of extraction process, Brunner and Esquivel model as kinetical model were used to fit the experimental data. Table 1 shows the yield and extraction rate for extraction of *Orthosiphon stamineus* by SC-CO_2.

Table 1. Calculated parameters for the Applied Mathematical Models (modified Brunner and Esquivel Models**)** and yield of *Orthosiphon stamineus* extracts.

T (°C)	P (bar)	yield (g)	Brunner model				Esquivel model			
			k_1(min)	extraction rate (g/min)	%AARD	R^2	k_1 (1/min)	extraction rate (g/min)	%AARD	R^2
					O. Stamineus leaves					
40	100	0.212	0.036	0.00763	4.354	0.997	12.363	0.0171	7.602	0.991
	300	0.286	0.0228	0.00653	5.346	0.991	25.149	0.0114	6.094	0.982
80	100	0.0364	0.0143	0.000521	14.661	0.987	60.247	0.000604	24.551	0.974
	300	0.4	0.0221	0.00884	7.146	0.995	34.541	0.0115	17.134	0.983
					O. Stamineus stems					
40	100	0.0945	0.0254	0.00240	3.636	0.993	29.185	0.00323	10.322	0.985
	300	0.186	0.0464	0.00870	5.621	0.988	10.632	0.0174	2.481	0.996
80	100	0.039	0.0209	0.000816	3.562	0.994	27.821	0.00140	10.766	0.975
	300	0.219	0.0399	0.00876	4.466	0.992	12.974	0.0169	4.052	0.995

The result shows that pressure at 300 bar and temperature 80 °C give the maximum yield of *Orthosiphon stamineus* leaves and stem extracts with maximum yield of leaves is 0.4 gram and stems is 0.219 gram. Increasing both pressure and temperature will increase the extract yield of both leaves and stem. The increase in pressure increases both the solvent density and solvation power of CO_2 to carry out the extract [24]. When the density of CO_2 increase, it will increase the interaction between CO_2 molecules and ethanol in the solvent will enhance the dissolution of *Orthosiphon stamineus* leaves and stem extracts [8]. Moreover, increase of pressure will also increase the power of solvent penetration, causing the matrices of raw material to be easily penetrated and broken by CO_2. Consequently, the solvent can easily carry out the extract from the broken matrices [25]. This result is comparable with findings that claimed increasing pressure will increase the yield of peanut skin oil by modified supercritical carbon dioxide [8, 26]. Pressure is a dominant variable to obtain high yield extract [27-29]. Furthermore, previous research has reported that the yield of virgin coconut oil was increased with the increase in the pressure of 31 MPa

to 34.5 MPa [30]. Moreover, addition of ethanol as co-solvent increases the polarity of solvent, where CO_2 as non-polar solvent is unable to extracts the polar compound. With addition of ethanol on the extraction process, the solvent can carry out polar and non-polar solvents [31, 32]. Increasing of temperature condition increases the yield of *Orthosiphon stamineus* leaves and stems extracts. Effect of vapour solute is dominant on the extraction process. Increasing of temperature will increase the vapour solute of *Orthosiphon stamineus* leaves and stems; hence, the extract is easily carried out. This is similar with the result from extraction of jack prain fruit by supercritical carbon dioxide, where increasing of temperature increase the jack prain fruit oil [11]. Determination of extraction rate for *Orthosiphon stamineus* leaves and stems extraction is compulsory to determine the behaviour and effect of parameters on the extraction process. Recently, Brunner and Esquivel Models as first order models are easily used to determine the extraction rate of extraction [19]. However, Brunner and Esquivel still fail to determine for extraction process that has low pressure condition below than 20 MPa.
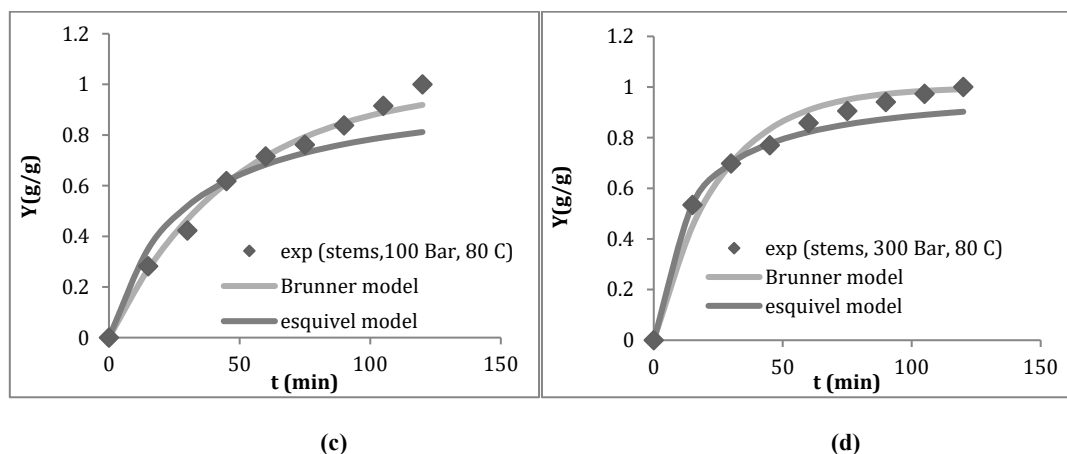
(a)

(b)

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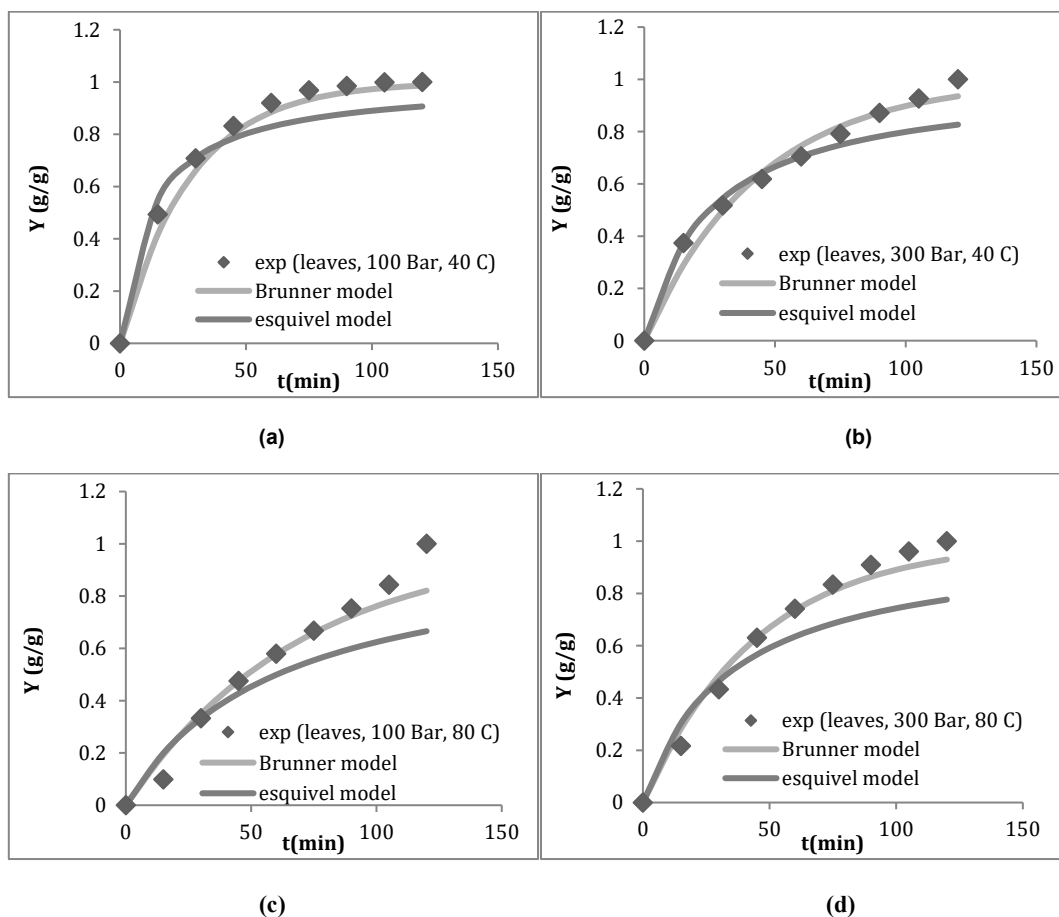
Fig. 3 Brunner and Esquivel model fitted at pressure (100 and 300 Bar) and temperatures (40 and 80 °C) on the extraction of *Orthosiphon stamineus* leaves.

Table 1 shows that Brunner model best fitted the *Orthosiphon stamineus* leaves extract with the lowest average % AARD 7.876% and R^2 0.993 compared with Esquivel model. Furthermore, the extraction rate is 0.000521 g/min to 0.00884 g/min. In addition, Fig. 3 shows that Esquivel and Brunner models fitted the experimental data of *Orthosiphon stamineus* leaves extraction at pressure (100 and 300 Bar) and temperature (40 and 80 °C). Fig. 3 reveals that Brunner and Esquivel models unsuccessfully fitted the experimental data of *Orthosiphon stamineus* leaves extraction at low pressure condition. This trend is similar with extraction of coriander seeds where the models had unsuccessfully correlate with the extraction process at low pressure condition [19]. This occurrence can be explained at low pressure condition, the graph of experimental data is usually linear, but an exponential trend occurred at high pressure condition. One of the dominant reasons is density of solvent. Increase in density allows better

extraction due to ability to penetrate deep in the sample matrix, thus increase the interaction between solute and solvents [33]. However, increase of temperature from 40 to 80 °C at constant pressure of 100 Bar decreases the extraction rate of *Orthosiphon stamineus* leaves. This is because increasing temperature decrease the density of solvent that will decrease the solvating power of solvent. There are fewer particles of CO_2 to interact with the extract inside of *Orthosiphon stamineus* leaves. However, at constant pressure of 300 Bar, increasing temperature from 40 to 80 °C will result in the increase in the leaves extraction rate. This is due to the effect of vapour solute is dominant of on the extraction process. Therefore, the extract can easily move from the raw material to the solvent. This result is similar with the previous findings where increasing temperature will increase the extraction rate of peanut skin oil by modified supercritical carbon dioxide [8].

(a)

(b)

(c)   (d)
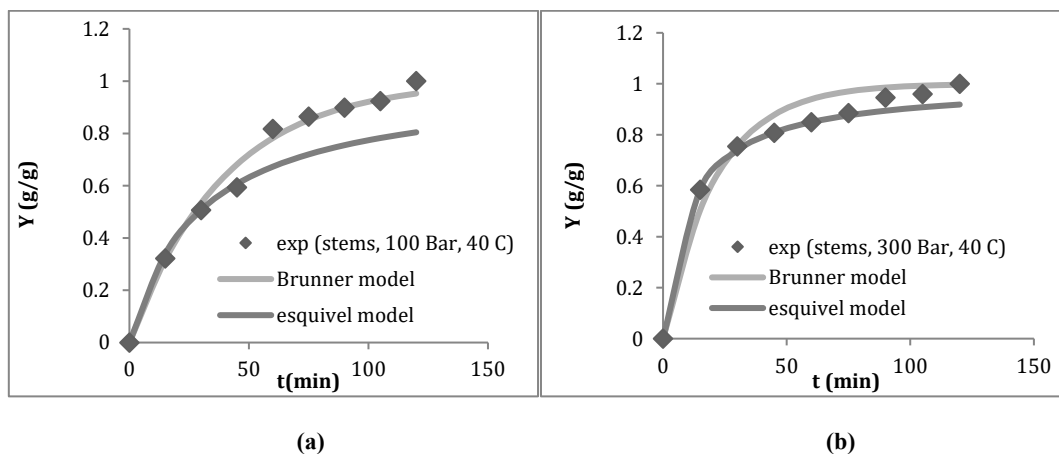
Fig.4 Brunner and Esquivel model fitted at Pressure (100 and 300 Bar) and temperatures (40 and 80 °C) on the extraction of *Orthosiphon stamineus* stems.

Similar to extraction *Orthosiphon stamineus* leaves, Brunner model also gives the best fitted to the experimental data on extraction of *Orthosiphon stamineus* stems with the lowest average AARD 4.321% and R^2 0.987 compared with Esquivel model. The extraction rate of extraction *Orthosiphon stamineus* stems is 0.000816 g/min to 0.00876 g/min. Furthermore, Fig. 4 shows that Esquivel and Brunner models fitted the experimental data of extraction of *Orthosiphon stamineus* stems at different pressure and temperature. It reveals that Brunner and Esquivel model does not fit the experimental data of extraction *Orthosiphon stamineus* leaves at low pressure condition. This trend is similar with extraction of coriander seeds where at low pressure (100 Bar), the models has unsuccessfully correlated with the extraction process [19]. Furthermore, increasing pressure will increase the extraction rate. This trend is similar with *Orthosiphon stamineus* leaves where the increasing pressure will increase the extraction rate. Therefore, both models and experimental have similar behaviours. One of the dominant reasons is density of solvent. Increasing of pressure will increase the density of solvent that has many interactions between carbon dioxide as a solvent and extract [33]. However, increasing of temperature from 40 to 80 °C at constant pressure 100 and 300 Bar decreases the extraction rate of *Orthosiphon stamineus* stems. This is because increasing temperature decrease the density of solvent that decrease the solvating power of solvent.

Comparison antioxidant activity between *Orthosiphon stamineus* stems and leaves

In this work, extraction of *Orthosiphon stamineus* leaves and stems were compared in terms of the quality of extracts.
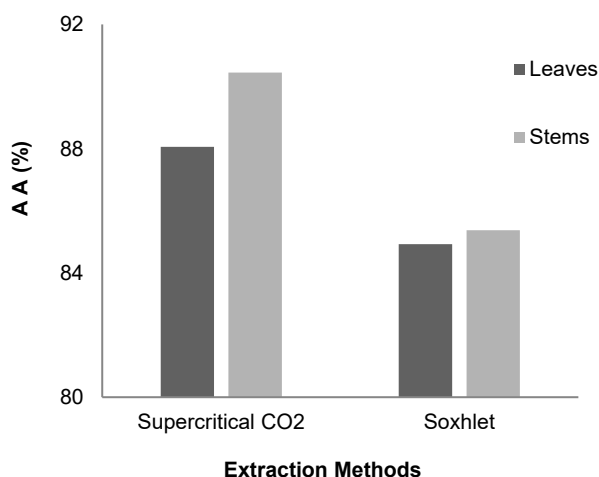
Fig. 5 Comparison of antioxidant activity extract obtained between supercritical carbon dioxide and Soxhlet extraction.

Fig. 5 illustrates the comparison of antioxidant activity in oil yield obtained from Soxhlet extraction and SC-CO$_2$ extraction at maximum yield of stems and leaves, where it clearly shows the significant value of antioxidant activity percentage for both extraction techniques. From the results obtained, SC-CO$_2$ extraction produced higher percentage of antioxidant activity compared to the Soxhlet extraction. Supercritical carbon dioxide extraction process used the lower temperature condition compared with the Soxhlet extraction. Low temperature condition prevents the degradation of bioactive compounds in the extract. The finding is similar with study on extraction of peanut skin oil where extraction using supercritical carbon dioxide gave higher antioxidant activity compared with Soxhlet extraction [24]. Moreover, extraction of *Piper betel* oil by supercritical carbon dioxide also gave higher antioxidant activity than Soxhlet extraction [28]. Furthermore, supercritical carbon dioxide is non-polar solvent that can easily extract the non-polar compounds in the *Orthosiphon stamineus* stems and leaves. Based on previous research, *Orthosiphon stamineus* stems and leaves contain high quantity of non-polar compounds such as sinensetin [2, 34-38]. Therefore, SC-CO$_2$ can easily extract out the solute. Based on this comparison, in order to obtain higher value of antioxidant activity in the global yield, SC-CO$_2$ extraction is the best method compared to Soxhlet extraction[39]. Antioxidant activity of *Orthosiphon stamineus* stems and leaves extract were 91.58% and 88%, respectively; showing that stems gave higher antioxidant activity compared to leaves. Moreover, both stems and leaves of *Orthosiphon stamineus* contain high bioactive compounds. This shows that *Orthosiphon stamineus* stems and leaves can be mixed as one raw material due to their similarity in extract quality. Therefore, the production cost can be reduced and the production of extract can be enhanced. Furthermore, Soxhlet extraction in this study has similar trends with the supercritical carbon dioxide due to the antioxidant of *Orthosiphon stamineus* stems and leaves extract. Antioxidant activity of *Orthosiphon stamineus* stems gives higher antioxidant activity (86%) compared with *Orthosiphon stamineus* leaves (85%).

CONCLUSION

In this study, Brunner and Esquivel model successfully correlated and fitted the experimental data of extraction Orthosiphon stamineus stems and leaves by supercritical carbon dioxide at pressure (10 and 30 MPa) and temperature (40 and 80 °C). The results show that Brunner model gives the better result of modelling compared with Esquivel model. The extraction rate of extraction of *Orthosiphon stamineus* stems is 0.000816 g/min to 0.00876 g/min with lowest average % AARD 4.321% and R^2 0.987. Furthermore, the extraction rate of *Orthosiphon stamineus* leaves extraction is 0.000521 g/min to 0.00884 g/min. with the lowest average % AARD 7.876 % and R^2 0.993. Moreover, increasing of pressure will increase the yield of extract and extraction rate due to the increase of density. This is because solvating power was enhanced by increasing of solvent density. Although Soxhlet extraction can give higher quantity of extract, supercritical

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carbon dioxide extraction can give higher antioxidant activity compared to Soxhlet extraction. In addition, *Orthosiphon stamineus* stems as zero-value raw materials give higher antioxidant activity compared with the leaves. Hence, *Orthosiphon stamineus* stems and leaves have not been separated due to similar high quality of extract. Therefore, the production costs can be reduced and the production of extract can be enhanced.

ACKNOWLEDGEMENT

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