Numerical model of supercritical fluid extraction CO_2 technique for cannabis extraction

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Abstract

This paper focuses on numerical modeling of cannabis extraction in supercritical fluid extraction (SFE) CO_2 process. First, two mathematical models, Sovova and Reverchon, are described. COMSOL program was used to solve numerical solution of both models. Then, verification of numerical models is shown. The extraction experiment was set up. Cannabis Savita L. oil was extracted in SFE CO_2 process. Extraction pressure and temperature conditions were 200 bars and 50°C, respectively. Numerical model was customized for Cannabis Savita L. To improve solution accuracy, total mass transfer was fitted from experimental data. RMS was used to optimize total mass transfer coefficient. Experimental results and the proposed numerical solutions were in a good agreement.

Key words

Supercritical fluid extraction CO_2, Numerical model, Cannabis, COMSOL, RMS

Introduction

In present, Cannabis is used in many medical treatments such as cancer, pain, Parkinson's disease, and other. Many researchers are interest to research new knowledge. By the way the extraction process for THC and CBD are many techniques [1] i.e. liquid-solid extraction, liquid-liquid extraction, cloud point extraction [2], supercritical fluid extraction, and others. Supercritical fluid extraction is one of many extraction processes to get a most purify extraction oils no contaminate.

The fluid above critical temperature and pressure is called a supercritical fluid. Supercritical fluid extraction of cannabis is pure and clean. This extraction method is one of the best extractions for pharmaceutical, food, and natural product. Extraction using carbon dioxide at supercritical conditions as it is non-toxic, non-flammable, and non-polluting. Properties of supercritical fluid are between gas and liquid phases. Merits of gas phase are low viscosity and great to diffuse through material. Carbon dioxide can touch every facial of material. Advantage of liquid phase is high density and great solute the material. It can be solute the material for many essential oils. These properties help to increase yield and quality more than another extraction method. Cannabis is one of herbs to study for medical. By the way, experimental for extraction only to analyze about particle size [3]. Other experiments study the effect of all parameters in extraction process [4]. They are no mathematical model to describe of cannabis sativa L. extraction.

To predict natural oil yield of supercritical fluid extraction process, broken and intact cell mathematical model was most successful. In 1994 Sovova proposed the broken and intact cell (BIC) model in solid phase to explain a physical phenomenon of oil extraction from vegetable seeds. Sovova develops the equations by applying mass transfer on the broken and intact cells. There are 3 exponential equations to describe 3 zones of extraction process i.e. fast zone, transition zone, and slow zone [5-6]. Sovova et al. [5-9] have described yield extraction of vegetable oil from seeds, essential oil from natural products i.e. grape seeds, almond seeds, pennyroyal leaves, lavender flowers, and orange peel. Her model required three adjustable parameters i.e.

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inaccessible oil concentration inside the product particle, mass transfer coefficient in CO_2 fluid phase and solid phase. These parameters require experimental data to fit their value. Other restriction of her model is hard to describe a holding process condition or near zero flow velocity of extractor because some parameters divide by mass flow rate. In 2001 Reverchon and Marrone have modified the BIC model in the form of the PDE and ODE equations [10]. The only one adjustable parameter, diffusion coefficient D_i, representing the internal mass transfer coefficient is required. His equations are flexible to use in many cases of extraction. Other merit of this model is able to predict a holding process condition of extractor.

COMSOL Multiphysics module is used in many porous flow simulations. Priyanka 2015 used COMSOL to solve Reverchon equations for supercritical extraction process of sage leaves. He referred parameters from Reverchon data and use COMSOL to solve PDE and ODE of carbon dioxide flow past sage particles [12]. The yield result is plotted to compare with experimental data.

The main objective of this study is modelling of cannabis extraction in supercritical fluid extraction CO_2 process. First mathematical models were explained. Then computational boundary conditions are described. RMS was applied to fit an adjustable parameter. Comparison of both mathematical models and experiment data of grape oil extraction are shown. Reverchon model is applied to predict oil yield of cannabis extraction in supercritical fluid extraction CO_2 process. The presented mathematical model has results in a good agreement with experimental results.

Materials and Methods

Mathematical and numerical modeling

In 1994 Sovova [5-6] approached BIC model to describe mass transfer behavior in fluid and solid phases. For fluid phase mass transfer rate equation is

$$\rho \varepsilon \frac{\partial y}{\partial t} + \rho U \frac{\partial y}{\partial h} = J(x, y) \tag{1}$$

While solid phase mass transfer rate equation is

$$-\rho_s (1 - \varepsilon) \frac{\partial x}{\partial t} = J(x, y) \tag{2}$$

where ρ is fluid density (kg/m³), ρ_s is solid density (kg/m³), ε is porosity, y is concentration in fluid phase, x is concentration in solid phase, U is superficial velocity (m/s), and t is time (s).

Mass transfer rate in fluid phase represents fast extraction zone. The first step of extraction in eq. (3a) is dependent on mass transfer rate in fluid phase only. Equation (3b) is a mass transfer rate equation of solid phase in slow extraction zone.

$$J(x > x_k, y) = k_f a_0 \rho (y_r - y) \tag{3a}$$

$$J(x \leq x_k, y) = k_s a_0 \rho_s x \tag{3b}$$

where k_f is mass transfer coefficient at fluid phase (m/s), k_s is mass transfer coefficient at solid phase (m/s), x_k is initial concentration inside the particle (kg oil/kg seed), y_r is solubility (kg oil/kg CO_2).

$$y_r = \left[\exp\left(40.361 - \frac{18{,}708}{T} + \frac{2{,}186{,}840}{T^2} \right) \times (0.001\rho)^{10.724} \right] / \rho \tag{4}$$

where T is temperature (K), ρ is density of CO_2, and y_r is the solubility of vegetable oil and is the common correlation initially fitted by de Valle et. al. [26].

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From the extended Lack's plug-flow model [5, 27], extraction curve is divided into 3 extraction zones (i) Fast zone, (ii) Transition zone, and (iii) Slow zone.

$$e = \begin{cases} qy_r[1 - \exp(-Z)] & for\ q < q_m\ :Fast\ zone \\ y_r[q - q_m\ exp(z_w - Z)] & for\ q_m \leq q < q_n\ :\ Transition\ zone \\ x_0 - \frac{y_r}{W}\ln\left\{1 + \left[exp\left(W\frac{x_0}{y_r}\right) - 1\right]exp[W(q_m - q)]\frac{x_k}{x_0}\right\} & for\ q_n \leq q\ :Slow\ zone \end{cases} \quad (5)$$

where e is the extraction yield i.e. the ratio of extraction weight and the mass of oil-free solid phase.

$$q_m = (x_0 - x_k)/y_r Z \quad (6)$$

$$q_n = q_m + \frac{1}{W}\ln\frac{x_k + (x_0 - x_k)\exp(Wx_0/y_r)}{x_0} \quad (7)$$

$$\frac{z_w}{Z} = \frac{y_r}{Wx_0}\ln\frac{x_0\exp[W(q - q_m)] - x_k}{x_0 - x_k} \quad (8)$$

$$Z = k_f a_0 \rho/[\dot{q}(1 - \varepsilon)\rho_s] \quad (9)$$

$$W = k_s a_0/[\dot{q}(1 - \varepsilon)] = kZy_r/x_k \quad (10)$$

Parameter Z is directly proportional to the fluid phase mass transfer coefficient and inversely proportional to the specific flow rate. Similarly, parameter W is directly proportional to the solid phase mass transfer coefficient and inversely proportional to the specific flow rate. $\dot{q}$ is specific flow rate (1/s), q_m and q_n is amount of CO_2.
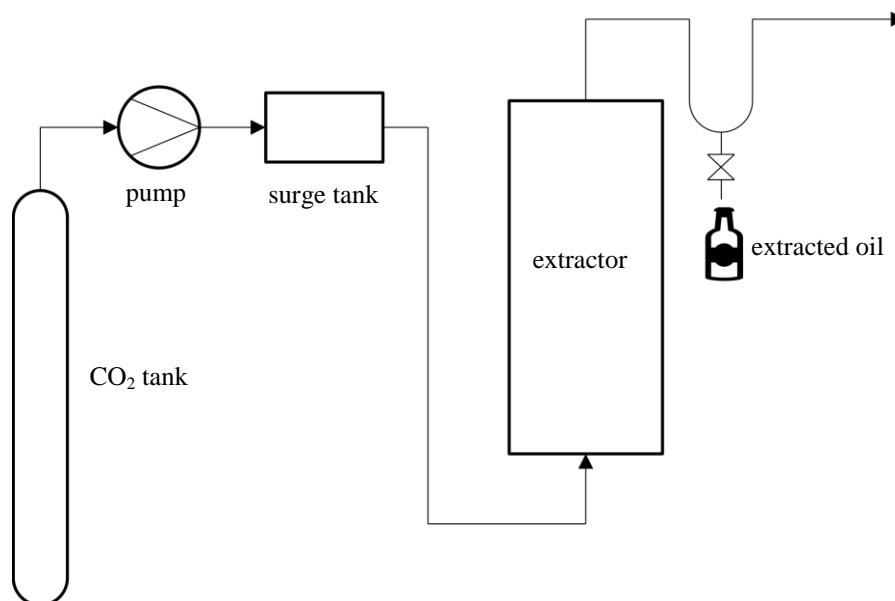

Figure 1: Scheme of the open-loop extraction process in down flow direction

Figure 1 shows lab scale and open-loop extraction. CO_2 from cylindrical tank supply to pump which increase pressure higher than critical pressure. Then high-pressure CO_2 flow into surge tank which constant pressure is maintained. Superficial CO_2 solvent flew up through the fixed bed in extractor. When CO_2 solvent

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interstitial velocity and the number of solid phases is small, the natural convection is dominated. Extraction phenomenon is explained by equation (5). The extracted oil is collected in a glass U tube.

For other product such as cannabis, non-vegetable and etc., this model requires to update an empirical equation i.e. equation 4 and three adjustable parameters i.e. inaccessible oil concentration inside the solid-phase particles x_k, mass transfer coefficient in CO_2 fluid phase k_f and solid phase k_s. These require an experimental data to fit their value. In case of no flow of CO_2 or holding process, this model cannot solve because parameter Z and W are inversely proportional to flow rate. Both parameters cannot solve from divide by zero.

Reverchon [10] also developed extraction equation from mass balance in two phases, fluid phase and solid phase. Mass balance equation in fluid phase is
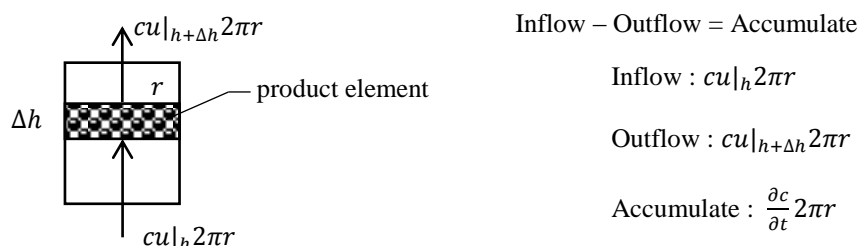

Inflow – Outflow = Accumulate

Inflow : $cu|_h 2\pi r$

Outflow : $cu|_{h+\Delta h} 2\pi r$

Accumulate : $\frac{\partial c}{\partial t} 2\pi r$

Figure 2: Mass flow consider in fluid phase

where c is the oil concentration in fluid phase, u is CO_2 fluid velocity, r is the radius of chamber, Δh is the height of product element.

While mass balance equation in solid phase is

Inflow – Outflow = Accumulate

Inflow : $\bar{c}K|_h 2\pi r$

Outflow : $\bar{c}K|_{h+\Delta h} 2\pi r$

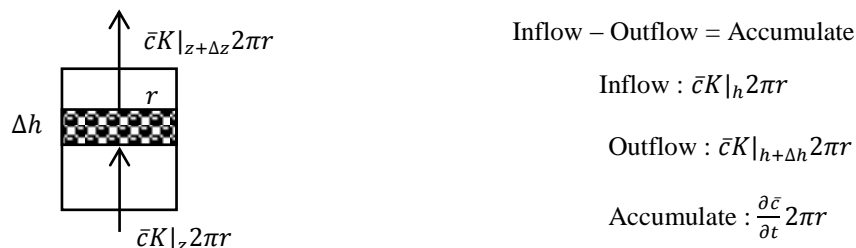Accumulate : $\frac{\partial \bar{c}}{\partial t} 2\pi r$

Figure 3: Mass flow consider in solid phase

where $\bar{c}$ is the oil concentration in solid phase, and K is mass transfer coefficient.

Apply Taylor series to solve mass balance equation. Then,

$$-\frac{\partial cu}{\partial h} = \frac{\partial c}{\partial t} \tag{11}$$

and

$$-\frac{\partial \bar{c}K}{\partial h} = \frac{\partial \bar{c}}{\partial t} \tag{12}$$

If u is constant and take V in fluid phase equation, eq. (11)

$$-uV\frac{\partial c}{\partial h} = V\frac{\partial c}{\partial t} \tag{13}$$

$$-uV\frac{\partial c}{\partial h} = \epsilon V\frac{\partial c}{\partial t} + (1-\epsilon)V\frac{\partial \bar{c}}{\partial t} \tag{14}$$

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PDE is
$$\epsilon V \frac{\partial c}{\partial t} + (1 - \epsilon)V \frac{\partial \bar{c}}{\partial t} + uV \frac{\partial c}{\partial h} = 0 \tag{15}$$

Take V in solid phase equation, eq. (12)

$$-KV \frac{\partial \bar{c}}{\partial h} = V \frac{\partial \bar{c}}{\partial t} \tag{16}$$

$$-KV \frac{\partial \bar{c}}{\partial h} = (1 - \epsilon)V \frac{\partial \bar{c}}{\partial t} \tag{17}$$

ODE is
$$-A_p K(\bar{c} - \bar{c}^*) = (1 - \epsilon)V \frac{\partial \bar{c}}{\partial t} \tag{18}$$

where c is concentration at fluid phase (kg/m^3), $\bar{c}$ is concentration at solid phase (kg/m^3), $\bar{c}^*$ is concentration at interface (kg/m^3) depending on the volumetric partition coefficient of the extract between the solid and the fluid phase at equilibrium, u is velocity in z axis (m/s), K is mass transfer coefficient (m/s), V is extractor volume (m^3), A_p is total particle area (m^2), t is time (s), ϵ is porosity.
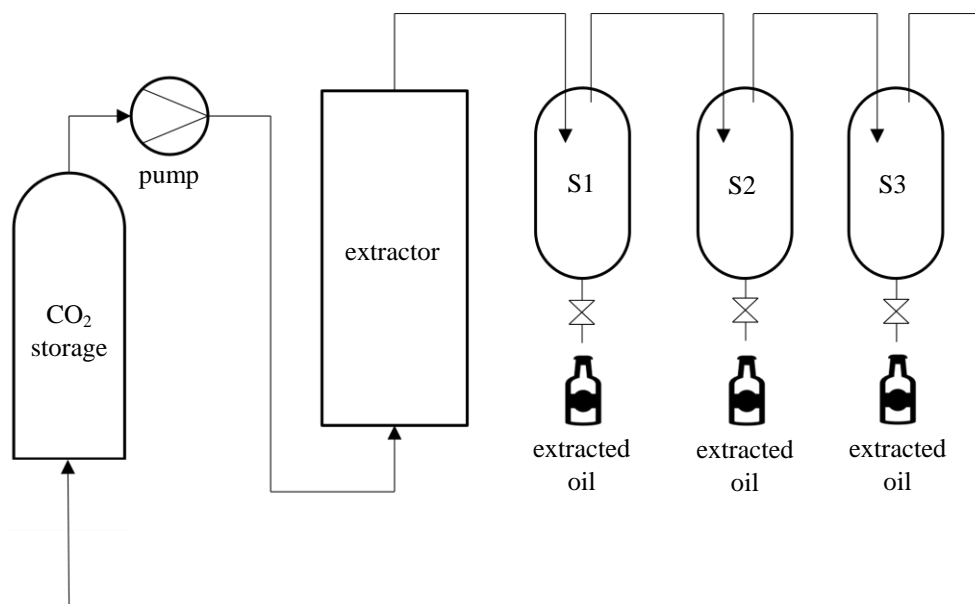

Figure 4: Scheme of the close-loop extraction process

Figure 4 represents pilot plant scale and the close-loop extraction with 3 separators. First CO_2 was full filled in the CO_2 storage. Pump increased solvent pressure more than critical pressure and passed thru a fixed bed in extractor. Then extracted oil was collected from separator 1, 2 and 3. After that solvent was returned to CO_2 storage and suctioned to pump again. Equation (15) and (18) are described the oil extraction phenomenon from both lab scale of open-loop extraction process with 2 separators and plant scale of close-loop extraction processes with 3 separators as well as neglect external mass transfer resistance.

Equation 15 requires velocity u in convective term. Darcy's law was used to solve velocity distribution and substituted in convective term of equation 15.

$$\frac{\partial}{\partial t}(\rho \epsilon) + \nabla \cdot (\rho u) = Q_m \tag{19}$$

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where ρ is the fluid density (kg/m^3), ϵ is the porosity, u is velocity, Q_m is mass source (kg/m^{3}s)

COMSOL Multiphysics

Equation 5 (Sovova model) can be solved by analytic function of COMSOL. While Coefficient Form PDE interface and Domain ODEs and DAEs were solved for equation 15 and 18 (Reverchon model), respectively.

Mathematical Modeling for cannabis extraction was considered in 1D problem. First Darcy's Law was applied to solve for velocity solution under fluid flow subgroup, Velocity results was then substituted in PDE and Domain ODEs and DAEs interfaces to obtain yield of extraction oil. For this study, Time dependent was applied to solve all equations.

Velocity distribution was solved from Darcy's law function through porous media. Boundary condition and initial condition are depicted in figure (5a).

B.C. at L = 0, Mass flux (0,t) = 80 (kg/h) / Cross-section Area

at L = 130, Pressure (130,t) = 200 bar

I.C. at t = 0, Pressure (L,0) = 50 bar

L = 130 mm, Temperature = 323.15 K, Porosity = 0.4, Permeability = 10^{-9} m^2

Concentration was simultaneously solved from Darcy's law (eq. 19), PDE (eq. 15) and ODE (eq. 18) Setting boundary condition and initial condition is describing in figure (3b).

B.C. at L = 0, c (0,t) = 0 (kg/m^3)

I.C. at t = 0, $\bar{c}$ (L,0) = $\bar{c}_0$ and c (L,0) = 0 (kg/m^3)

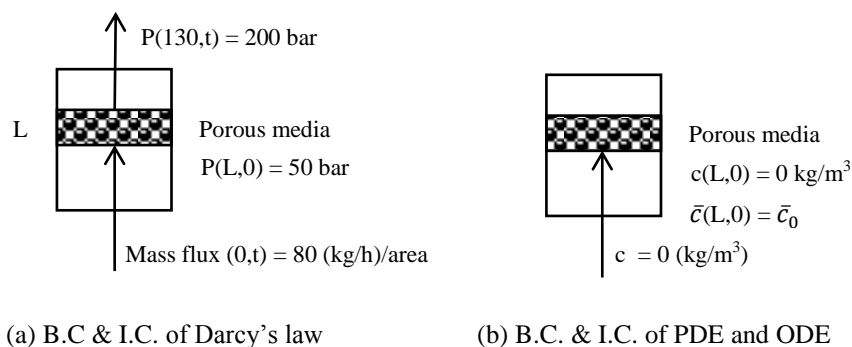(a) B.C & I.C. of Darcy's law   (b) B.C. & I.C. of PDE and ODE

Figure 5: Schematic representation of extraction bed

Above equations are solved for $\bar{c}$ at outlet of extractor ($\bar{c}$ (130,t)). Solid concentration from L = 0 to L = 130 was accumulated and measured at L = 130 mm. COMSOL first solves the Darcy's law to get velocity by time. Then velocity is substituted in PDE and ODE to solve oil concentration by time dependent. Result is plotted between yield and time.

Experiment of cannabis extraction

Cannabis sativa L. flower from north-east of Thailand was used in this study. Cannabis is dried by oven 24 hours with moisture around 6-7% by weight. Particle size for experimental is 0.25 mm. Dried cannabis 200 grams was packed in cylinder extractor 400 ml. and porosity 40%. Supercritical fluid extraction (SFE) process

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of cannabis is extracted in close-loop cycle. This experiment was setup at Thammasat University Center of Excellence in Computational Mechanics and Medical Engineering, Thammasat University, Thailand.

In this study SFE system has a fixed-bed cylindrical extractor and two separators. CO_2 flow from CO_2 tank into storage then pump up into extraction chamber at pressure $P_x = 200$ bar and temperature $T_x = 50$ ^{o}C above critical point of CO_2 ($P_{cr} = 73.8$ bar, $T_{cr} = 31.1$ ^{o}C). After that pressure and temperature were droppe8d at separator 1 ($P_{s1} = 150$ bar, $T_{s1} = 50$ ^{o}C) and separator 2 ($P_{s2} = 60$ bar, $T_{s2} = 30$ ^{o}C). Then CO_2 return to storage as close loop cycle. Cannabis oil was collected at separator 1 and 2 every 30 minutes. The results are plotted between yield (extraction oil/oil concentration) and time.

Result and Discussion

Supercritical fluid extraction CO_2 of grape oil [6] is used to study and compare the results of two mathematical models and experimental data. Extractor pressure and temperature were controlled to 280 bar and 40.0^{o}C, respectively. Extraction time is 307 minutes. Dried grape seeds contained 12.6 wt% oil and 6.8 wt% water and was milled with four grades 1 – 4 prior to loading into the extractor as shown in figure 1. The specific flow rate was varied from 3.8×10^{-3} s^{-1} (18.6 mg/s) to 59.5×10^{-3} s^{-1} (38 mg/s) were done by changing the grape seed from 0.6 to 5.6 grams.

Figure 2 represents experiment data of the up-flow extractor 150 ml with two specific flow rates : Case A 4.8×10^{-3} s^{-1} (29.28 mg/s) and case B 17×10^{-3} s^{-1} (29.92 mg/s). Grape seed weigh 6.1 grams in case A and 1.75 grams in case B. Equation 5 represented by Sovova was used to predict extracted yield. Based on data from her experiment, Sovova fitted several parameters in equation 5. Sovova curve are closely to experiment data. Proposed model was modified from Reverchon equation and used for the close-loop and up flow extractor 400 ml with 2 or 3 separators. Proposed model will first solve Darcy's law to obtain velocity field. Then velocity was substituted in Reverchon equations (PDE equation 15, and ODE equation 18) to solve for yield solution. Proposed curve was plotted in figure 6. One parameter, mass transfer coefficient K, in equation 18 was fitted by experiment A. The proposed model uses total mass transfer coefficient K_{total} instead of internal mass transfer coefficient K_{int}. K_{total} represents the overall mass transfer behavior in linear form of internal mass transfer coefficient K_{int} and external mass transfer coefficient K_{ext}.

$$K_{total} = K_{int} + K_{ext} \tag{20}$$

Then equation 18 was changed to support this idea.

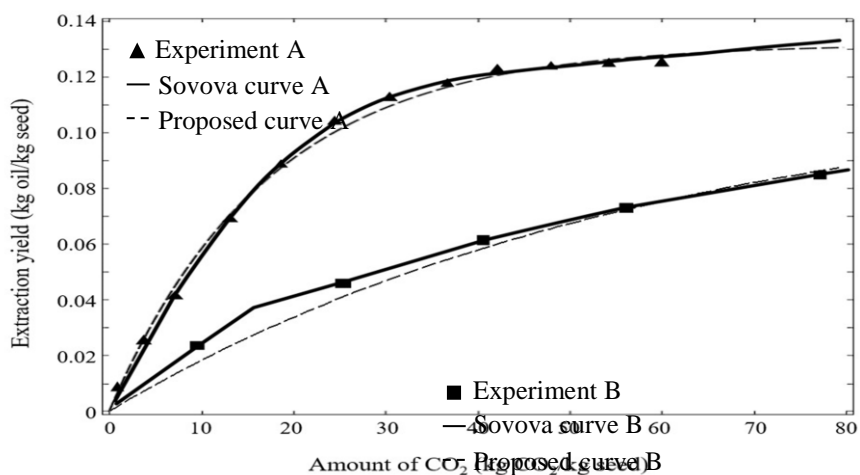$$-A_p K_{total}(\bar{c} - \bar{c}^*) = (1 - \epsilon)V \frac{\partial \bar{c}}{\partial t} \tag{21}$$

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Figure 6: Yield comparison of experiment, Sovova and proposed models at mass flow rate 18.6 mg/s.

In this study, K_{total} , 1.4×10^{-8} m/s, was evaluated and fitted from experiment data of case A and used to predict yield in case B. The proposed curve obviously shows C^0 and C^1 continuity of solution curve and true error is about 3% while Sovova fitting curve has one kink point at 15 kg CO_2/kg seed and 0.036 kg oil/kg seed as well as expresses only C^0 continuity of solution curve. From this result, the proposed model shows better potential of generalized model in extraction process than Sovova model.

The proposed model was then used to predict supercritical fluid extraction CO_2 of cannabis oil. Cannabis was extracted 2 times as shown in figure 8 at pressure 200 bars and temperature $50^{\circ}C$. Each batch consumed 180 minutes and collected extraction oil every 30 minutes. Figure 8 depicts concentration oil (%w/w) in y axis and time in x axis.
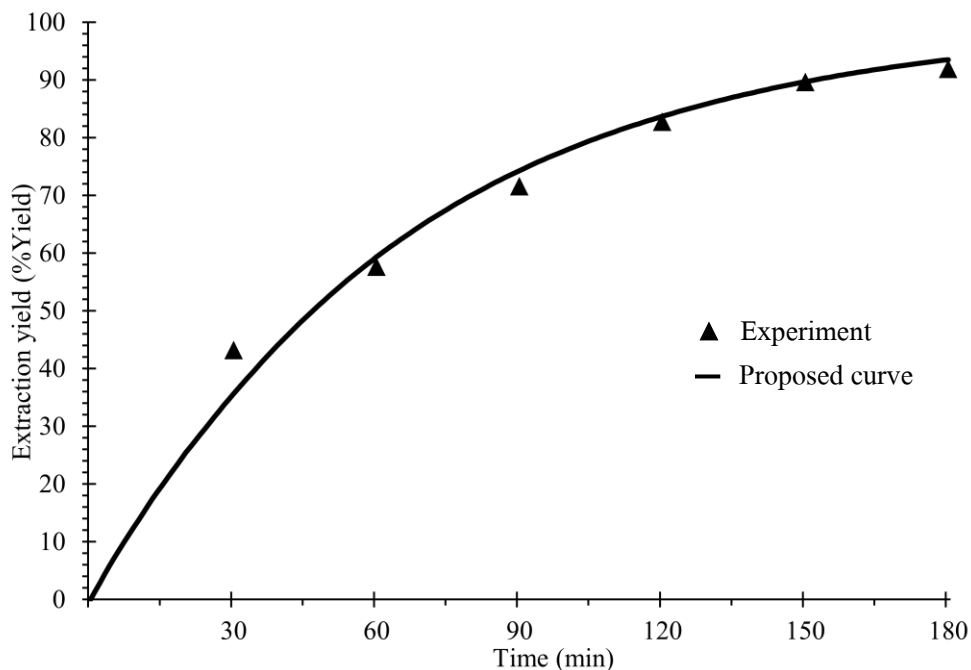

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Figure 8. Concentration oil of experiment

Experiment data in figure 8 were used to find total mass transfer coefficient. RMS model was presented to minimize error. Experimental data was recorded every 30 minutes until total time e 180 minutes and was calculated in RMS model, equation 22.

$$RMS = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(Model_i - Exp_i)^2} \tag{22}$$

Figure 9 shows a fitting curve of total mass transfer coefficient in MATLAB. It expresses RMS value in y axis and total mass transfer coefficient in x axis.

Curve equation is in polynomial 2nd order form.

$$y = ax^2 + bx + c \tag{23}$$

$$a = 1.0487 \times 10^2$$

$$b = -2.2307 \times 10^2$$

$$c = 122.08$$

Take derivative in equation 23 to obtain minimum value of RMS ($y' = 0$)

$$y' = 2(1.0487 \times 10^2)x - 2.2307 \times 10^2 \tag{24}$$

Substitute $y' = 0$, then

$$0 = 2(1.0487 \times 10^2)x - 2.2307 \times 10^2$$

$$x = 1.0636 \text{ x } 10^{-8} \text{ m/s}$$

Total mass transfer coefficient 1.0636×10^{-8} m/s is then used to solve yield of cannabis oil extraction in supercritical fluid extraction CO_2.

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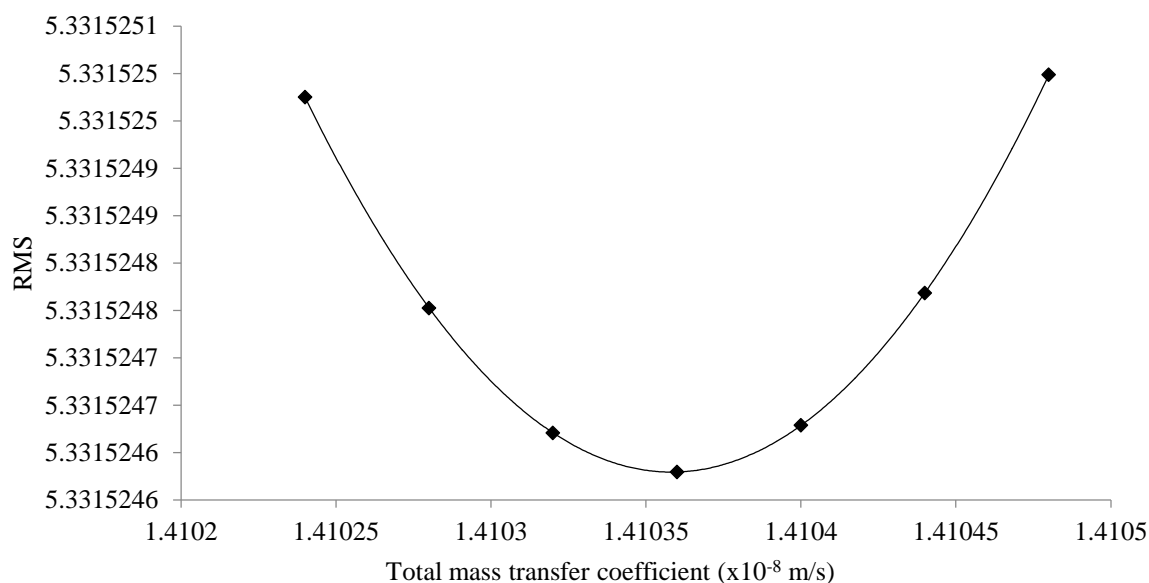Eur. Chem. Bull. 2023, 12(Special Issue 6),7354- 7364

Figure 9. Total mass transfer coefficient vs RMS

Results of a proposed model are compared with experimental data as shown in figure 9. Results are computed considering RMS of experimental data and plotted between extraction yield and extraction time. The extraction oil from a proposed model has a good agreement with experimental data. The true error is 4.55%. The parameters used in proposed equations are suitable for extract simulation of Cannabis Sativa L.

Conclusion

This study presents a proposed model consisting of Darcy's law to solve for fluid velocity and modified Reverchon model. Mass transfer coefficient is changed to be total mass transfer coefficient. It is the linear summation of internal and external mass transfer coefficients and is evaluated from experimental data and RMS model.

Grape oil extraction from supercritical fluid extraction CO_2 process was used to verify the capability of a proposed model comparing with experimental data and Sovova model. The results show that a proposed model is more general application than Sovova and have a good agreement with experimental data.

Cannabis Sativa L oil was extracted from a close-loop supercritical fluid extraction CO_2 process under pressure 200 bars and temperature $50^{o}C$ in this study. Results from a proposed model are close to experiment data with error 4.55%. Total mass transfer coefficient is only one material property requirement in a proposed model. This paper shows that a proposed model is a general model and have a good agreement with experimental data both of grape oil extraction and cannabis oil extraction from supercritical fluid extraction CO_2.

Reference

1. Adejoke H. T., Louis, H., Amusan O. O., Apebende G., *A Review on Classes, Extraction, Purification and Pharmaceutical Importance of Plants Alkaloid*, Journal of Medicinal and Chemical Sciences, **2019**, 2(4), pp. 130-139.
2. Jassem I. A., Abdul-Hassan W. S., Flafel I. A., A. Ali S. A., Mahdi Z. M., *Cloud Point and Solvent Extraction of Copper (II) by Bis (3-chloro acetylacetone) Ethylenediamine*, Journal of Medicinal and Chemical Sciences, **2022**, 5(6), pp. 988-1000.
3. Lél EÖRY, Béla DÁNOS, Tibor VERESS, *Supercritical Fluid Extraction of Tetrahydrocannabinol from Marihuana Study of The Effect of Particle Size,* Problems of Forensic Sciences, **2001**, 47, pp. 322-327.
4. Laura J. Rovetto, Niccolo V. Aieta, *Supercritical carbon dioxide extraction of cannabinoids from Cannabis sativa L,* Journal of Supercritical Fluids, **2017**, 129, pp. 16-27.
5. Sovova H., *Rate of the vegetable oil extraction with supercritical CO2-I modeling of extraction curves*, Chemical Engineering Science, **1994**, 49(3), pp. 409-414.
6. Sovova H., Kucera J., Jez J., *Rate of the vegetable oil extraction with supercritical CO2–II extraction of grape oil*, Chemical Engineering Science, **1994**, 49(3), pp. 415-420.
7. Sovova H., *Steps of supercritical fluid extraction of natural products and their characteristic times*, The Journal of Supercritical Fluids, **2012**, 66, pp. 73 – 79.
8. Sovova H., *Mathematical model for supercritical fluid extraction of natural products and extraction curve evaluation*, The Journal of Supercritical Fluids, **2005**, 33, pp. 35 – 52.
9. Helena Sovova, Anatolii A. Galushko, Roumiana P. Stateva, Kristina Rochova, Marie Sajfrtova, Milena Bartlova, *Supercritical fluid extraction of minor components of vegetable oils: b-Sitosterol*, journal of food engineering, **2010**, 101, pp. 201 – 209.
10. E.Reverchon, *Mathematical Modeling of Supercritical Extraction of Sage Oil,* AIChE Journal, **1996**, 42(6), pp. 1765-1771.
11. E.Reverchon and I. De Marco, Supercritical fluid extraction and fractionation of natural matter, The Journal of Supercritical Fluids, **2006**, 38, pp. 146 – 166.
12. Priyanka, Shabina. Khanam, *Simulation of Supercritical Fluid Extraction Process Using COMSOL Multiphysics*, **2015**.
13. Cussler, E. L., *Fundamentals of Mass Transfer,* Cambridge University Press, New York, England, **1997**.
14. Cussler, E. L., *Diffusion: Mass Transfer in Fluid Systems (2nd ed.),* Cambridge University Press, New York, England, **1997**.
15. F. Mills, *Heat and Mass Transfer,* University of California at Los Angeles, United States of America, **1995**.
16. Richard W. Johnson, *The Handbook of Fluid Dynamics,* Idaho National Engineering, Idaho, USA, **1998**.
17. M. Spiro, M. Kandiah. *Extraction of ginger rhizome: partition constants and other equilibrium properties in organic solvents and in supercritical carbon dioxide,* International Journal of Food Science & Technology, **1990**, 25(5), pp. 566-575.
18. Ting May Lin, Then Siew Ping, Agus Saptoro, Panau Freddie, *Mass Transfer Coefficients and Correlation of Supercritical Carbon Dioxide Extraction of Sarawak Black Pepper*, International Journal of Food Engineering, **2013**, 10(1), pp. 1-15.
19. Wuttichai Jaidee, Ittipon Siridechakorn, Siwames Nessopa, Vanuchawan Wisuitiprot, Nathareen Chaiwangrach, Kornkanok Ingkaninan, and Neti Waranuch, *Kinetics of CBD, Δ 9 -THC Degradation and Cannabinol Formation in Cannabis Resin at Various Temperature and pH Conditions*, Cannabis and Cannabinoid Research, **2021**, 7 (4), pp. 537-547.
20. Karin Tomita, Siti Machmudah, Armando T. Quitain, Mitsuru Sasaki, Ryuichi Fukuzato, Motonobu Goto, *Extraction and solubility evaluation of functional seed oil in supercritical carbon dioxide*, Journal of Supercritical Fluids, **2013**, 79, pp. 109-113.
21. Helena Sovova and Roumiana P. Stateva, *Supercritical fluid extraction from vegetable materials*, Reviews in Chemical Engineering, **2011**, 27(3-4), pp. 79–156.
22. Penny Whiting, Et al. (2017). *Cannabinoids for Medical Use A Systematic Review and Meta-analysis,* JAMA The Journal of the American Medical Association, **2017**, 313(24), pp. 2456-2473.
23. E. Munson, L. S. Harris, M. A. Friedman, W. L. Dewey, and R. A. Carchman, *Antineoplastic Activity of Cannabinoids,* Journal of the national cancer institute, **1975**, 55 (3), pp. 597-602.
24. E.Reverchon, *Modeling of Supercritical Fluid Extraction from Herbaceous Matrices*, Industrial and Engineering Chemistry Research, **1996**, 32 (11), pp. 2721-2726.
25. Priyanka KatiyarKaran GuptaPushpraj KatiyarShabina Khanam, *Supercritical fluid extraction of turmeric root oil using CO2: Experimental banalysis and process modelling*, Industrial Crops & Products, **2022**, 188, 115559.
26. de1 Valle J. M., and Aguilera. J. M., *An Improved Equation for Predicting the Solubility of Vegetable Oils in Supercritical Co₂*, Industrial and Engineering Chemistry Research, **1988**, 27(8), pp. 1551–1553
27. Lack, E. A., Kriterien zur Auslegung von Anlagen fiir die Hochdruckextraktion von Naturstoffen. Ph.D. thesis, **1985**, TIJ Graz.

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