The Journal of Supercritical Fluids 133 (2018) 42–48

Contents lists available at ScienceDirect

The Journal of Supercritical Fluids

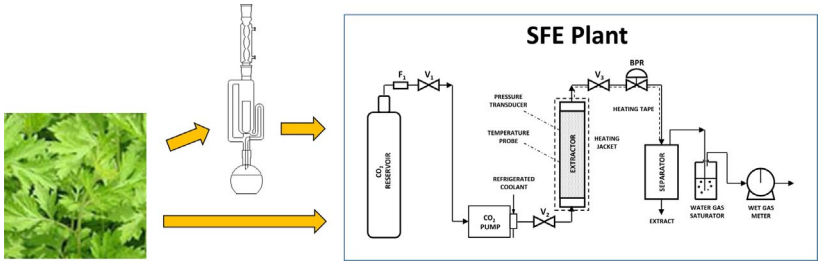
journal homepage: www.elsevier.com/locate/supflu

Desorption of artemisinin extracts of CIM-Arogya by supercritical carbon dioxide

Arvind Singh Negi[a], Angelo Cortesi[b,*], Ireneo Kikic[b], Alberto Bertucco[c], Massimo Calabrese[d], Dario Solinas[b]

[a] CIMAP, Council of Scientific and Industrial Research, 226015 Lucknow, India
[b] DIA, Department of Engineering and Architecture, University of Trieste, Via A. Valerio 6/a, 34127 Trieste, Italy
[c] DII, Department of Industrial Engineering, University of Padova, Via G. Gradenigo 6/A, 35131 Padova, Italy
[d] DEAMS, Department of Economics, Management, Mathematics and Statistics, University of Trieste, Via A. Valerio 6, 34127 Trieste, Italy

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Artemisinin
Supercritical carbon dioxide
Soxhlet extraction
Supercritical desorption

ABSTRACT

Artemisinin is a drug for chloroquine resistant malaria and cerebral malaria treatments. In the recent past, there was an acute shortage of this drug and hence World Health Organization made a strategy to fulfil the Artemisinin demand.

In this study, artemisinin was extracted by supercritical Carbon Dioxide ($SFCO_2$) from CIM-Arogya, a variety of Artemisia annua, in temperature and pressure ranges of 313.1-333.1 K and 15–25 MPa. Artemisinin global yield isotherms were determined obtaining a maximum yield of 3.65 wt%. Artemisinin extracts were also obtained by hexane Soxhlet extraction: then, the crude extracts were purified using $SFCO_2$, after adsorption on silica gel. Different desorption runs were performed with a 6 ml/min CO_2 flow rate, in temperature and pressure ranges of 313.1–333.1 K and 15–25 MPa. At different time intervals, extracts were collected and analysed: their yields varied from 2.75% to 4.34% function of the experimental conditions. Desorption trials were also correlated with different models.

1. Introduction

Isolated from the aerial parts of Artemisia annua (Family: Asteraceae), artemisinin, a sesquiterpene lactone, and its derivatives are powerful medicines known for their ability to swiftly reduce the number of Plasmodium parasites in the blood of patients with malaria. This drug has been developed from the Chinese traditional medicine and is known as Qinghaosu.

The World Health Organization as the first-line treatment for uncomplicated Plasmodium falciparum malaria recommends Artemisinin-based combination therapies (ACTs). Expanding access to ACTs in malaria-endemic countries has been integral to the remarkable recent

* Corresponding author.
E-mail address: angelo.cortesi@dia.units.it (A. Cortesi).

http://dx.doi.org/10.1016/j.supflu.2017.09.024
Received 25 July 2017; Received in revised form 21 September 2017; Accepted 22 September 2017
Available online 23 September 2017

success in reducing the global malaria burden. In 2015, 311 million ACT treatment courses were procured by endemic countries – up from 187 million in 2010 [1].

Further optimization of artemisinin-based therapy for malaria is ongoing. A number of semisynthetic routes to prepare artemisinin analogues such as artemether and artesunate with changes to the d-lactone portion have been developed with the goal of improving the pharmacokinetic properties. New combination therapies in which one of the components is an artemisinin-derived antimalarial either are in clinical development or recently approved therapies [2].

In addition to natural artemisinin and dihydroartemisinin, the semisynthetic artemisinin derivatives artemether, arteether, and artesunate have been increasingly used for about 20 years. These drugs are metabolized to dihydroartemisinin, the main bioactive compound. The artemisinins act faster than any other antimalarial drugs, with an approximate parasite- and fever-clearance time of 32 h, in contrast to 2–3 days needed with conventional antimalarial drugs to resolve the symptoms. To shorten the treatment duration and to prevent the development of resistance, the artemisinins are progressively associated with other antimalarial drugs with longer half-lives.

Although the total synthesis of artemisinin has been realised, its product is not yet competitive in price with the natural one, because of its high abundance in the plant (0.6–1.2%). Due to the use of artemisinin as such and its chemical modification to various semisynthetic drugs, there is a high demand of this compound in pharmaceutical industry. Presently, liquid solvent extraction with hexane, petroleum ether, and toluene is the most applied technique. However, these procedures exhaust a large amount of potentially hazardous solvents to the environment, and its recovery yield is low. Therefore, alternative extraction technique with better selectivity and efficiency are highly desirable.

Artemisinin solubility in supercritical carbon dioxide ($SFCO_2$), in terms of mole fraction, was found to range from 10^{-4} to 10^{-3}, which is higher than typical solubilities of many biological molecules [3–5].

Quispe-Condori et al. [6], in 2005, report the global yield isotherms and the kinetic of extraction from Artemisia annua leaves using $SFCO_2$. They obtained the maximum yield of 5.7% at 323.1 K and 30 MPa, with artemisinin purity in the extracts around 12 wt%. Lin et al. [7], at 323.1 K and 173.4 MPa, achieve higher purity values of 73 wt%, with a total yield of 0.5%.

Some papers report supercritical carbon dioxide artemisinin extractions, from Artemisia annua L., by adding co-solvents: 3% of methanol at 150 bar and 40 °C by Kohler et al. [8,9], 16.25% of *n*-hexane at 70–208 bar and 40–60 °C by Lin et al. [7] and 16.25% of ethanol at 173–311 bar and 40–60 °C by Tzeng et al. [10]. The co-solvent modified $SFCO_2$ extraction produces more pure artemisinin than classical Soxhlet solvent extraction.

Martinez-Correa et al. [11], in 2017, introduce a process with two-step extractions of bioactive compounds present in Artemisia annua L. They use $SFCO_2$ in the first step and ethanol or water in the second one (on the solid residue of the supercritical extraction). The conclusion is that in the supercritical extraction most of the artemisinin is extracted and therefore a second extraction step it is not necessary. Recently, an interesting article reports the supercritical fractional extraction of Artemisia annua L., producing extracts enriched in Artemisinin [12]. The work demonstrates the efficiency of the fractional cooling separation that allows complete elimination of waxes that confer solid or semi-solid consistency to SFE extracts.

From the comparison between the different extraction techniques [7–9,11] it seems that the solvent extraction with hexane still gives the better results in terms of total yields.

A combination of extraction with traditional organic solvents and supercritical carbon dioxide desorption is proposed, in some cases, for the obtainment of high purity extracts from natural sources. Guyer et al. [13] recover onion flavour from onion juice by adsorption and $SFCO_2$ desorption from polymeric adsorbent. Braida et al. [14] obtain greater antioxidants concentration from labiatae family herbs. In their work, crude oleoresins, obtained from dried leaves of rosemary using organic solvents, are used as starting material. Supercritical extraction of oleoresin followed by an adsorption step with various adsorbents is carried out. After adsorption, retained compounds are recovered in a desorption step under the same supercritical condition but using ethanol as co-solvent.

The first part of this work concerns the direct artemisinin $SFCO_2$ extraction from CIM-Arogya, a variety of Artemisia annua. In the second part a simplified solvent extraction-$SFCO_2$ desorption approach is applied: after a Soxhlet plant extraction, with hexane, the crude extracts are directly coated with silica gel and the solvent removed under vacuum. Then the supercritical carbon dioxide is used only in the desorption step. Several desorption conditions are studied and correlated with different models. All the obtained extracts are analysed by HPLC technique.

2. Materials and methods

2.1. Materials

The Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow India, developed a variety of Artemisia annua, named CIM-AROGYA. This variety is characterized by the high content of artemisinin ranging from 1 to 1.2%. The raw material was dried at 40 °C, in a tray drier with air circulation (Memmert Universal Oven UF30, Germany), and comminuted. The resulting material packed in a plastic bottle placed in a freezer.

The particle size distribution was determined using a vibratory sieve shaker (Giuliani, Turin, Italy): different mesh size of sieves (35, 40, 50, 60, 80 and 100) were taken and arranged in a tower shape.

Particles from 35 to 60 meshes were selected for the extraction experiments.

The real density of the particles was measured by helium gas pycnometry (Ultrapycnometer-1000, Quantachrome Instruments – USA) and is of 1030.0 kg/m^3.

Carbon dioxide with a purity of 99.98% was purchased by Società Italiana Acetilene e Derivati (SIAD, Italy). Hexane pro analysis grade and Silica gel 60–120 mesh (Merck) were used in the organic extraction and in the desorption process, respectively.

In HPLC analysis the used methanol and absolute ethanol were purchased by Sigma-Aldrich.

2.2. Experimental procedures

2.2.1. Supercritical fluid extraction

The supercritical fluid extraction of the plant material was performed in the LAB SFE 100 ml, from Separex, that is composed of a CO_2 heater, an extractor with extraction cells of different volumes, a temperature and pressure control system, and an extract collector [15].

The extraction unit is designed for operation up to 50 MPa and 423.1 K. Liquefied CO_2 from the reservoir is cooled (Haake K cooling bath) and pumped by a dual-piston pump (Lewa EKM210V1). Pressure is controlled with a heated back-pressure regulator (Tescom 26-1762-24-043).

Ten grams of dry material, with an artemisinin content of 1.2 wt%, were charged in the extraction cell. The same procedure was repeated for all the experiments.

Flow rate of carbon dioxide was maintained constant in all the runs at 25 g/min.

The influence of extraction temperature and pressure was investigated in the range 313.1–333.1 K and 15–25 MPa. Samples were collected at different time intervals (from 10 to 90 min).

2.2.2. Supercritical fluid desorption

The supercritical fluid desorption assays were executed on raw CIM-

AROGYA extracts coated with silica gel. The organic solvent extraction was carried out at Central Institute of Medicinal and Aromatic Plants using hexane as a solvent. Raw material was grounded and contacted with the solvent in a conventional Soxhlet apparatus. The ratio (wt/wt) between the feed of raw material and hexane was 1:4. The extracts were mixed with fixed amount of silica gel (20% of extract over the adsorbent), and treated in a rotary evaporator under vacuum at 313.1 K to remove the solvent. The final material after the total removal of the solvent was conserved in a sealed bottle maintained in a refrigerator. From this container the amount for each desorption experiment was taken.

The Lab SFE 100 ml apparatus was also used for the desorption steps. The extraction cell was filled in the bottom with glass particles, in order to homogeneously distribute the carbon dioxide flow, and in the upper part with the raw organic extracts coated in silica gel. 12 g of supported material were introduced and a flow rate of 6.2 g/min was maintained in the different desorption tests. The experimental conditions and procedures were similar to those used in the extraction of artemisinin from plant material.

2.2.3. HPLC quantification of the extracts

The HPLC equipment consisted of a Spectra System P2000 pump with an SCM 100 vacuum membrane degasser and an electrochemical detector 2465 (Waters, MA, USA), with glassy carbon electrode (3-mm in diameter), potential 180 mV, 200 nA. Samples were injected with a model 7125i sample valve equipped with a 20 µl loop (Rheodyne, Rohnert Park, CA, USA). Separations were carried out with a Supelco Discovery, RP-C18 (25 cm × 4,6 mm; 5 µm i.d.) reversed phase column (Supelco, Bellefonte, PA, USA) equipped with a Supelco Pelliguard LC-18 2 cm precolumn (Supelco). The eluents were distilled water (A) and methanol (B). The mobile phase was isocratic, using 50%A and 50%B for 15 min at a flow rate of 1 ml/min. The system operated with oven temperature of 303.1 K.

Calibration curves were obtained from an ethanolic dilution series of the reference standards containing artemisinin. Concentrations ranging between 5 and 50 mg/l of artemisinin were prepared, from the standard stock dilution, by serial dilution with ethanol for the calibration data. Calibration levels (n = 5) were measured six times. Linear regression was used to establish the calibration curve. Results were calculated using the peak areas by means of Chromcard software (Thermoquest).

3. Results and discussion

3.1. Supercritical fluid extraction

At low pressure of 15 MPa the global yield diminishes with increasing temperature (Fig. 1) whereas at the highest pressure

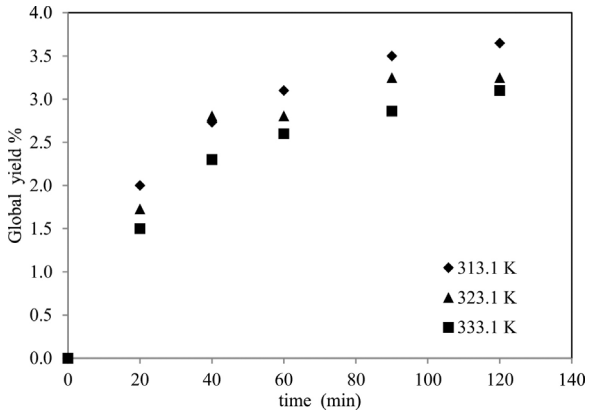


Fig. 1. Extraction from plant, effect of temperature at 15 MPa.

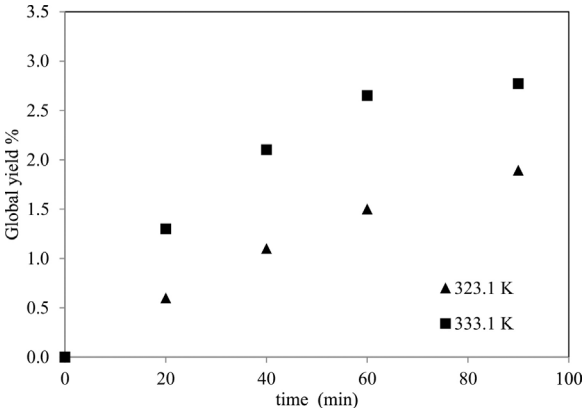


Fig. 2. Extraction from plant, effect of temperature at 25 MPa.

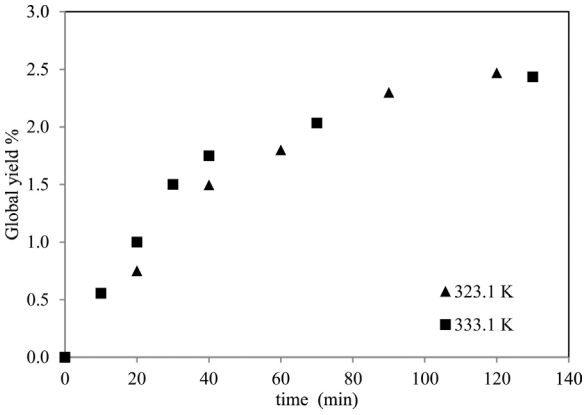


Fig. 3. Extraction from plant, effect of temperature at 20 MPa.

investigated of 25 MPa (Fig. 2) the temperature has a positive effect on yield.

At intermediate pressure values, the global yield is almost constant with temperature (Fig. 3) confirming the data obtained by Quispe-Condori et al. [6]. They observed that the global yield obtained at 303.1 K is higher of that obtained at 323.1 K for pressures lower than a crossover pressure situated approximately at 200–220 MPa. In the case of the lower temperature the yield increases with pressure until 15 MPa and after it remains constant whereas at 323.1 K the yield increases with pressure.

The maximum yield of 3.65 wt%, is obtained at 313.1 K and 15 MPa. This value is comparable to that obtained by Quispe-Condori et al. [6].

The variation of the artemisinin purity with time agrees with the results of literature [6]: it decreases with time in all the extraction conditions: higher purity is obtained in the fractions collected between 20 and 30 min. In Table 1 the artemisinin purity at 30 min is reported. The maximum purity (22%) is obtained at temperature of 333.1 K and pressure of 25 MPa.

3.2. Supercritical fluid desorption

The analysis of hexane extracts, used as starting materials for the

Table 1
Artemisinin% purity after 30 min of extraction from plant material.

	15 MPa	20 MPa	25 MPa
313.1 K	8.0	3.0	4.0
323.1 K	6.0	14.5	8.0
333.1 K	9.5	19.5	22.0

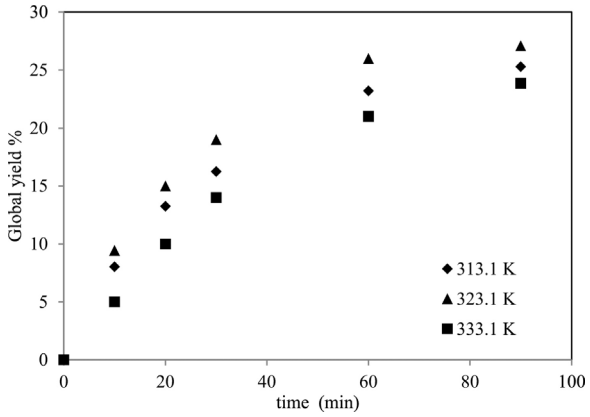


Fig. 4. Desorption yield, effect of temperature at 15 MPa.

desorption, reports an artemisinin content of 17.3 wt%. No detailed analysis of these extracts was performed and therefore the exact content of the different components is not known. Nevertheless, from the results reported in literature [6,7,10], waxes, different sesquiterpenes and camphor are reasonably present.

The experimental conditions, temperatures and pressures, for desorption are the same as that used for the extraction from raw material.

At 15 and 20 MPa (Figs. 4 and 5) the global yield decreases when the temperature decreases from 323.1 to 313.1 K whereas the lowest yields are obtained at 333.1 K. At the highest pressure investigated (25 MPa, Fig. 6) again the maximum yield is obtained at 323.1 K respect to those at 313.1 and 333.1 K that show similar values.

The global yield always increases with the pressure, as reported in Fig. 7 for desorption runs at 333.1 K.

The global yields data after 90 min, reported in Table 2, confirm the behaviour outlined in the figures: a maximum value of 46.3% is obtained at 323.1 K and 25 MPa, whereas at 20 MPa and at the same temperature, a slowly lower yield of 38.7% is realized.

For a comprehensive comparison of the results achieved in the different experimental conditions, Table 3 reports the Artemisinin concentration data (purity%) after 10 min. The maximum concentrations are obtained operating at 20 MPa for all the temperatures considered. The higher concentration value is 84 wt%, and it is reported operating at 20 MPa, and 323.1 K and 333.1 K. At these conditions, the variation of the artemisinin purity, in the fractions collected at different desorption times, is reported in Fig. 8. For both temperatures, the purity decreases with time, reaching values below 20 wt% after 90 min. Following the isotherm at 323.1 K, after a faster decrease at the beginning, the concentration at the end is higher respect to the data at 333.1 K. Similar behaviour is observed also at other pressures. In all the collected fractions the lower concentrations are obtained at 313.1 K.

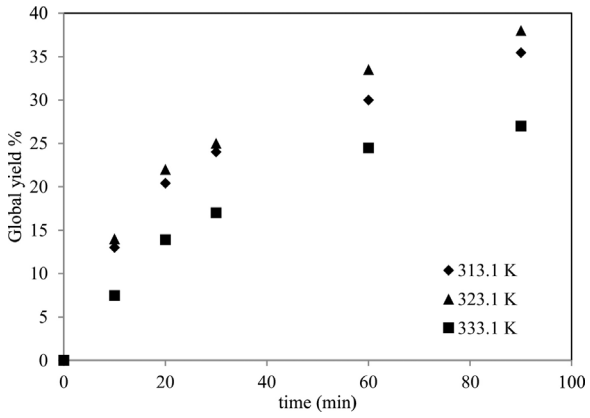


Fig. 5. Desorption yield, effect of temperature at 20 MPa.

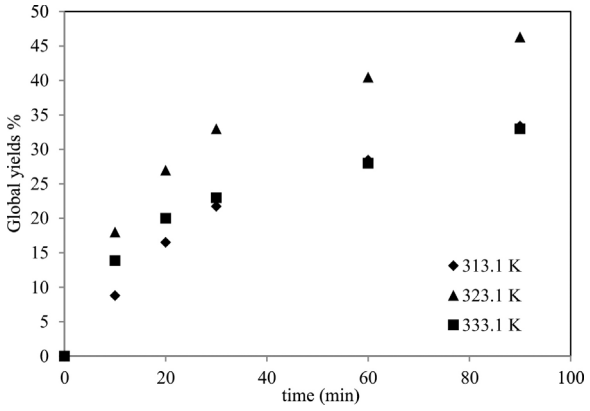


Fig. 6. Desorption yield, effect of temperature at 25 MPa.

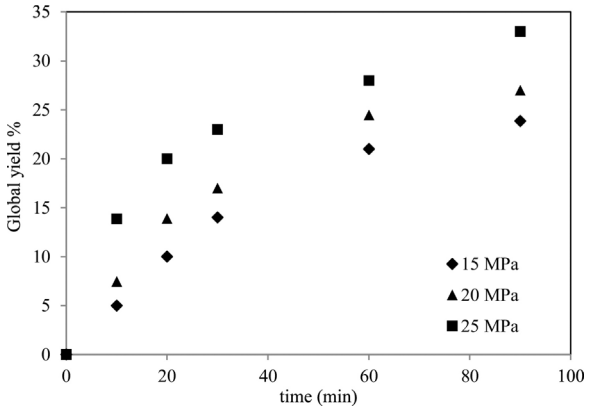


Fig. 7. Desorption yield, effect of pressure at 333.1 K.

Table 2
Global yields% in the desorption trials at 90 min.

	15 MPa	20 MPa	25 MPa
313.1 K	25.2	35.3	34.3
323.1 K	27.1	38.7	46.3
333.1 K	23.8	27.0	33.0

Table 3
Artemisinin% purity in the desorption trials at 10 min.

	15 MPa	20 MPa	25 MPa
313.1 K	30.0	38.0	35.0
323.1 K	70.0	84.0	32.0
333.1 K	53.1	84.0	24.0

It is interesting also to evaluate the average Artemisinin concentrations, reported in Table 4, after 90 min. These values, corresponding to one hypothetical fraction for the entire 90 min, are lower than those obtained for any single fraction. The best average concentration is achieved operating at 333.1 K and 20 MPa.

The recovery of artemisinin was also evaluated. The variation of artemisinin yield with pressure at 333.1 K, reported in Fig. 9, is similar to the trend of the global yield: rising the pressure from 15 to 20 MPa there is a net increase of the yield obtaining a good recovery of the artemisinin initially contained in the crude hexane extracts.

The effect of temperature on the artemisinin yield also shows a similar behaviour to that obtained for the total yield of desorption. In Fig. 10, for the supercritical trials at 20 MPa, the lower yield is achieved at 313.1 K whereas the maximum value is obtained at the intermediate temperature of 323.1 K. This apparently anomalous effect of

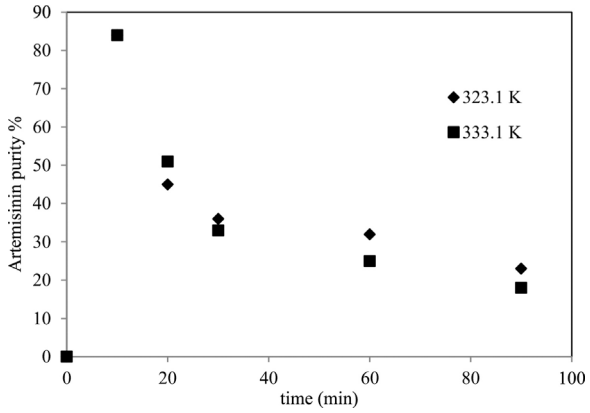


Fig. 8. Artemisinin concentration, effect of temperature at 20 MPa.

Table 4
Average% concentration of Artemisinin (after 90 min) in the desorption trials.

	15 MPa	20 MPa	25 MPa
313.1 K	18.0	23.8	28.6
323.1 K	29.0	33.9	23.0
333.1 K	31.8	44.9	25.0

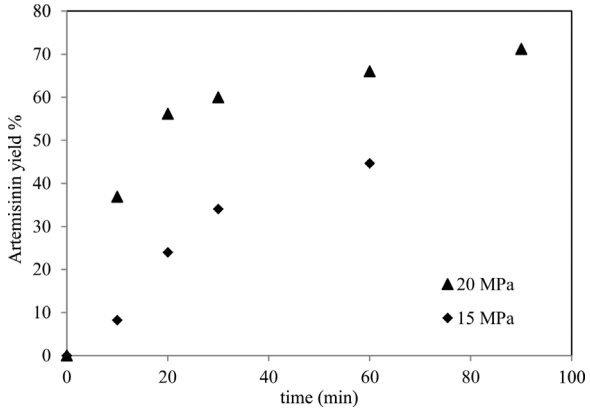


Fig. 9. Artemisinin yield, effect of pressure at 333.1 K.

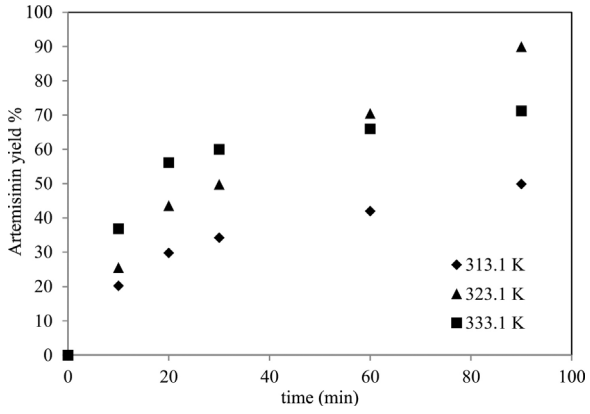


Fig. 10. Artemisinin yield, effect of temperature at 20 MPa.

temperature was carefully investigated by triplicate the extraction isotherms at 323.1 K.

In Table 5 the artemisinin yields after 60 min are reported for the different experimental conditions. The yield increases for all the temperatures from 15 to 20 MPa and then decreases reaching at 25 MPa a value close to that of the lower pressure investigated. In the average,

Table 5
Artemisinin yields% in the desorption trials at 60 min.

	15 MPa	20 MPa	25 MPa
313.1 K	35.4	42.1	38.0
323.1 K	58.8	70.5	61.2
333.1 K	44.7	66.0	47.7

the best values are obtained for all the pressures at the temperature of 323.1 K. The maximum recovery is 70.5% reached at 323.1 K and 15 MPa.

The focus of the investigation was the evaluation of the artemisinin recovery and for this reason no attention was payed to the analytical determination of the other compounds present in the extracts. It is obvious that their presence influences the solubilisation of artemisinin and its recovery.

A more detailed analysis of these results can be done taking into account that the desorption behaviour is the result of the balance between mass transfer and thermodynamic. At the present we have some elements only for the evaluation of the diverse interactions between the different components present in the matrices, carbon dioxide and adsorbent.

No extensive data for the adsorption of the pure components are found except for artemisinin.

Xing et al. [16] measure the adsorption of artemisinin on silica gel. The important observation is that adsorbed quantity enhances increasing temperature and decreasing pressure. From this result it is possible to extrapolate the effect of the temperature and pressure on the opposite process of desorption.

The same adsorbent, but with different particle sizes, is used in the present research. For this reason it is possible to conclude that probably the quantity of artemisinin desorbed will decrease increasing temperature and decreasing pressure if the artemisinin is the only solute adsorbed. Unfortunately, there are no quantitative data for other compounds co-desorbed.

As mentioned before also the interactions of the different solutes with carbon dioxide are important. An indication on these interactions can be derived from data on solubility of the different component in carbon dioxide.

Starting from the literature results about the analysis of the extracts obtained from the leaves of Artemisia annua [6,12], a careful search for the solubility data of the different components in carbon dioxide was done. Solubility data only for artemisinin, camphor and heavy hydrocarbons (waxes) in carbon dioxide [3–5,17–19] were found. These data concerns only the binary system of these compounds with carbon dioxide and no data on multicomponent systems were found.

Camphor is the main component accompanying artemisinin but the data reported in [12] reveal that also other sesquiterpenes are present. This is very important since these compounds have a chemical structure similar to that of the artemisinin and probably their behaviour in presence of carbon dioxide is also qualitative the same.

The artemisinin data in the range 308.1–328.1 K show an inversion point at approximately 19 MPa. The camphor solubility data reported in [17–19] exhibit an inversion solubility behaviour at lower pressure (7.5 MPa).

From the comparison of the pure components behaviour, the camphor presents the higher solubility in carbon dioxide. Nevertheless from the data reported in [8], when there are coextracted from leaves of Artemisia, apparently there is an inversion of the behaviour and artemisinin yields are definitively much higher than those of camphor. For these reasons camphor and the other compounds, with a structure close to that of artemisinin, enhance the solubility of artemisinin modifying the solubility behaviour of the pure compound.

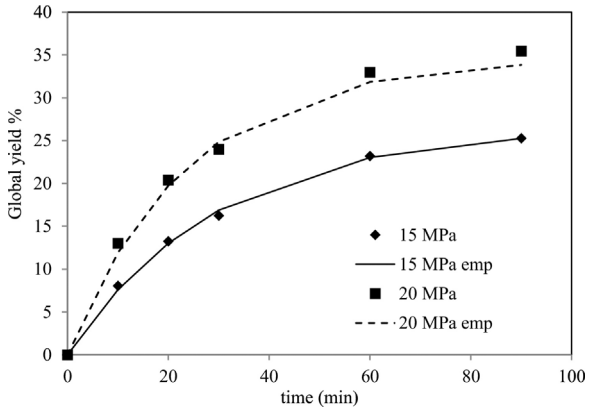


Fig. 11. Empirical modelling of desorption at 313.1 K.

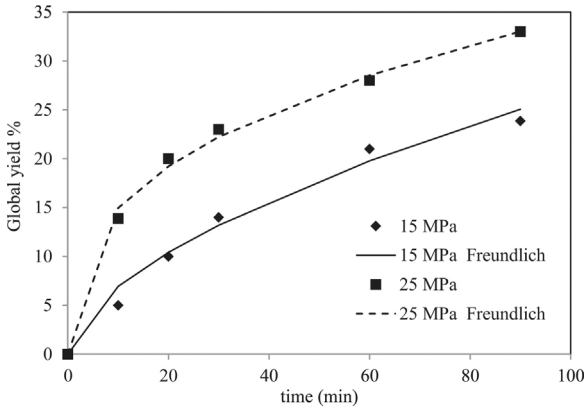


Fig. 12. Freundlich modelling of desorption data at 333.1 K.

3.3. Desorption modelling

Many approaches have been used to modeling supercritical desorption processes [20–27] also due to the increasing interest in using this technique for the purification of natural materials [13,14,28–32].

A pure empirical approach for the correlation of desorption data, obtained in the study of the recovery of onion flavours, suggests the following equation [13]:

$$Y = b_1[1 - \exp(-b_2 t)] \tag{1}$$

where b_1 and b_2 are empirical constant obtained by fitting of the experimental data. In Fig. 11 the correlation results, obtained for the desorption at 313.1 K, are reported: the modeling lines reproduce very well the experimental data.

The other models are developed considering the adsorption equilibrium and mass transfer resistance. Equilibrium theory, which assumes that mass transfer resistance are negligible, is the simplest method of describing the measured desorption data and have been used by several authors [22,23,26]. When equilibrium theory is applied to isothermal, fixed bed, plug flow desorption, the desorption profile will be a function of the adsorption equilibrium relationship. The behaviour of an adsorber can be described by Eq. (2) when equilibrium is assumed [33]:

$$t = \frac{L}{u}\left[1 + \left(\frac{1-\varepsilon}{\varepsilon}\right)\frac{dq}{dc}\right] \tag{2}$$

where dq/dc is the slope of the adsorption isotherm, L is the length of the bed, u the velocity and ε is the void fraction in the packed column.

This equation is used to develop an expression for the breakthrough curve for the desorption of a uniformly saturated bed with a pure carrier. The derivative term dq/dc is obtained from the relevant adsorption isotherm expression and after integration an equation describing the desorption profile can be obtained:

$$\left(\frac{\partial z}{\partial t}\right)_c = \frac{v}{1 + \left(\frac{1-\varepsilon}{\varepsilon}\right)\frac{dq}{dc}} \tag{3}$$

where z is the axial position in the column.

Freundlich and Langmuir adsorption isotherm were used following the approach outlined.

As an example in Fig. 12 the results obtained using the Freundlich isotherm are reported for the desorption data at 333.1 K. The agreement is quite good. Similar agreements are also obtained using the Langmuir isotherm for the desorption data at 323.1 K reported in Fig. 13. The two models give quite similar desorption isotherm behaviors.

The assumption of local equilibrium is probably not fully justified and the different approach suggested by Tan and Liou [24–26] was also tested.

The three approaches were applied to model the experimental desorption profiles.

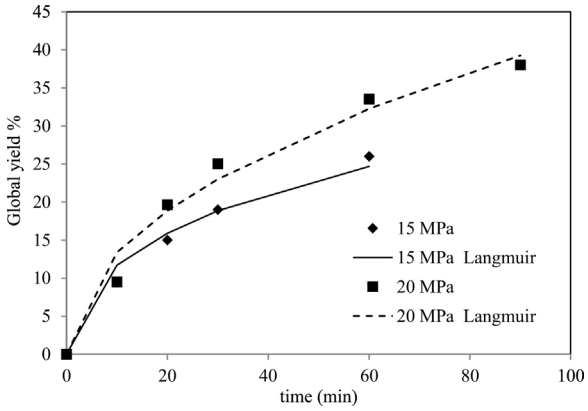


Fig. 13. Langmuir modelling of desorption data at 323.1 K.

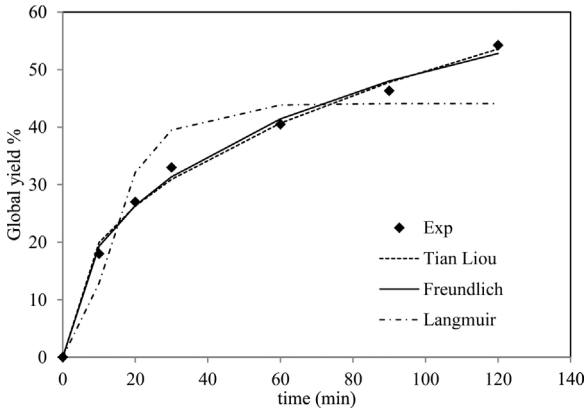


Fig. 14. Desorption profiles calculated with different models (experimental conditions of 323.1 K and 25 MPa).

As an example in Fig. 14 the comparison between the fraction desorbed determined experimentally and that obtained by correlation with the three models is presented.

The profiles obtained using the Freundlich and Langmuir isotherms are similar and larger deviations are showed by the Tan and Liou equation.

It is interesting to observe that also the adsorption data for pure artemisinin on silica gel [17] were correlated with the Freundlich model with excellent results.

4. Conclusions

The present study investigates the use of supercritical carbon dioxide to extract artemisinin, directly from the leaves of Artemisia annua and by desorption from organic fractions obtained with hexane extraction.

In the supercritical fluid extraction process, the global yield exhibits different performances with pressure and temperature: at 15 MPa diminishes with T whereas, at 25 MPa, its value increases with T. At intermediate P values the global yield is almost constant with temperature, confirming a crossover behaviour at pressures close to 19 MPa. In the studied experimental ranges, the maximum yield of 3.65 wt%, is obtained at 313.1 K and 15 MPa.

Finally, the higher Artemisinin purity is obtained in the fractions collected between 20 and 30 min, at elevated P and T values (25 MPa and 333.1 K).

In the supercritical desorption process the global yields increase with pressure.

The artemisinin yield report the highest values at 20 MPa and 323.1 K and the lowest at 15 MPa and at all the temperatures. The artemisinin concentration of the desorbed extracts is very high at the beginning of the desorption process reaching a value of 84% operating at 20 MPa and at the temperatures of 323.1 K and 333.1 K for the fractions collected in the first 10 min.

Desorption trials were correlated with different models and better and similar results were obtained with Freundlich and Langmuir isotherms.

The results obtained encourage a further experimental investigation on mass transfer effects in order to design a real two-step process for the production of artemisinin.

Acknowledgements

The authors gratefully acknowledge Dr. G. Longo, past-president of ICS-UNIDO Trieste, for his scientific support.

References

[1] World Health Organization, Malaria: Q & A On Artemisinin Resistance, (2017) March http://who.int/malaria/media/artemisinin_resistance_qa/en/ (Accessed 10 May 2017).
[2] N. Gogtay, U.M. Thatte, P.L. Olliaro, D. Sinclair, Artemisinin-based combination therapy for treating uncomplicated Plasmodium vivax malaria, Cochrane Database Syst. Rev. 10 (2013), http://dx.doi.org/10.1002/14651858 (CD008492.pub3).
[3] H. Xing, Y. Yang, B. Su, M. Huang, Q. Ren, Solubility of Artemisinin in supercritical carbon dioxide, J. Chem. Eng. Data 48 (2003) 330–332.
[4] P. Coimbra, M.R. Blanco, H.S.R. Costa Silva, M.H. Gil, H.C. de Sousa, Experimental determination and correlation of artemisinin's solubility in supercritical carbon dioxide, J. Chem. Eng. Data 51 (2006) 1097–1104.
[5] X.-Y. Gong, X.-J. Cao, Measurement and correlation of solubility of artemisinin in supercritical carbon dioxide, Fluid Phase Equilib. 284 (2009) 26–30.
[6] S. Quispe-Condori, D. Sánchez, M.A. Foglio, P.T.V. Rosa, C. Zetzl, G. Brunner, M.A.A. Meireles, Global yield isotherms and kinetic of artemisinin extraction from Artemisia annua L. leaves using supercritical carbon dioxide, J. Supercrit. Fluids 36 (2005) 40–48.
[7] Y.-L. Lin, C.-C. Yang, H.-K. Hsu, S.-L. Hsu, C.-M.J. Chang, Response surface methodology to supercritical fluids extraction of artemisinin and the effects on rat hepatic stellate cell in vitro, J. Supercrit. Fluids 39 (2006) 48–53.
[8] M. Kohler, W. Haerdi, P. Christen, J.-L. Veuthey, Supercritical fluid extraction and chromatography of artemisinin and artemisinic acid. An improved method for the analysis of Artemisia annua samples, Phytochem. Anal. 8 (1997) 223–227.
[9] M. Kohler, W. Haerdi, P. Christen, J.-L. Veuthey, Extraction of artemisinin and artemisinic acid from Artemisia annua L. using supercritical carbon dioxide, J. Chromatogr. A 785 (1997) 353–360.
[10] T.-C. Tzeng, Y.-L. Lin, T.-T. Jong, C.-M.J. Changa, Ethanol modified supercritical fluids extraction of scopoletin and artemisinin from Artemisia annua L, Sep. Purif. Technol. 56 (2007) 18–24.
[11] H.A. Martinez-Correa, R.G. Bitencourt, A.C.A. Kayano, P.M. Magalhães, F.T. Costa, F.A. Cabral, Integrated extraction process to obtain bioactive extracts of Artemisia annua L. leaves using supercritical CO2, ethanol and water, Ind. Crops Prod. 95 (2017) 535–542.
[12] L. Baldino, E. Reverchon, G. Della Porta, An optimized process for SC-CO2 extraction of antimalarial compounds from Artemisia annua L, J. Supercrit. Fluids 128 (2017) 89–93.
[13] D.E. Guyer, C. Saengcharoenrat, C.T. Lira, Onion flavor recovery in the process of adsorption and supercritical carbon dioxide desorption, J. Food Proc. Eng. 28 (2005) 205–218.
[14] I. Braida, M. Mattea, D. Cardarelli, Extraction–adsorption–desorption process under supercritical condition as a method to concentrate antioxidants from natural sources, J. Supercrit. Fluids 45 (2008) 195–199.
[15] N. De Zordi, A. Cortesi, I. Kikic, M. Moneghini, D. Solinas, G. Innocenti, A. Portolan, G. Baratto, S. Dall'Acqua, The Supercritical carbon dioxide extraction of polyphenols from Propolis: a central composite design approach, J. Supercrit. Fluids 95 (2014) 491–498.
[16] H. Xing, B. Su, Q. Ren, Y. Yang, Adsorption equilibra of artemisininfrom supercritical carbón dioxide on silica gel, J. Supercrit. Fluids 49 (2008) 189–195.
[17] M. Akgun, N.A. Akgun, S. Dincer, Phase behaviour of essential oil components in supercritical carbon dioxide, J. Supercrit. Fluids 15 (1999) 117–125.
[18] R.N. Carvalho Jr., M.L. Corazza, L. Cardozo-Filho, M.A.A. Meireles, Phase equilibrium for (camphor + CO_2), (camphor + propane), and (camphor + CO_2 + propane), J. Chem. Eng. Data 51 (2006) 997–1000.
[19] R.B. Gupta, J.-J. Shim, Solubility in Supercritical Carbon Dioxide, CRC Press, Boca Raton, FL, 2007.
[20] S. Lucas, M.P. Calvo, J. García-Serna, C. Palencia, M.J. Cocero, Two-parameter model for mass transfer processes between solid matrixes and supercritical fluids: analytical solution, J. Supercrit. Fluids 41 (2007) 257–266.
[21] M.J. Cocero, J. García, Mathematical model of supercritical extraction applied to oil seed extraction by CO_2 + saturated alcohol—I. Desorption model, J. Supercrit. Fluids 20 (2001) 229–243.
[22] R.P. de Filippi, V.J. Krukonis, R.J. Robey, M. Modell, Supercritical fluid regeneration of activated carbon for adsorption of pesticides, Report EPA-600/2-80054 March, (1980) (Washington D.C.).
[23] G. Madras, C. Erkey, A. Akgerman, Supercritical fluid regeneration of activated carbon loaded with heavy molecular weight organics, Ind. Eng. Chem. Res. 32 (1993) 1163–1168.
[24] C.-S. Tan, D.-C. Liou, Desorption of ethyl acetate from activated carbon by supercritical carbon dioxide, Ind. Eng. Chem. Res. 27 (1988) 988–991.
[25] C.-S. Tan, D.-C. Liou, Supercritical regeneration of activated carbon loaded with benzene and Toluene, Ind. Eng. Chem. Res. 28 (1989) 1222–1226.
[26] C.-S. Tan, D.-C. Liou, Modeling of desorption at supercritical conditions, AIChE J. 35 (1989) 1029–1031.
[27] F. Recasens, B.J. McCoy, J.M. Smith, Desorption processes: supercritical fluid regeneration of activated carbon, AIChE J. 35 (1989) 951–958.
[28] D. Chouchi, D. Barth, E. Reverchon, G. Della Porta, Supercritical CO_2 desorption of Bergamot peel oil, Ind. Eng. Chem. Res. 34 (1995) 4508–4513.
[29] P. Subra, A. Vega-Bancel, E. Reverchon, Breakthrough curves and adsorption isotherms of terpene mixtures in supercritical carbon dioxide, J. Supercrit. Fluids 12 (1998) 43–57.
[30] L. Danielski, G. Brunner, C. Schwänke, C. Zetzl, H. Hense, J.P.M. Donoso, Deterpenation of mandarin (Citrus reticulata) peel oils by means of countercurrent multistage extraction and adsorption/desorption with supercritical CO_2, J. Supercrit. Fluids 44 (2008) 315–324.
[31] A.S. Negi, G. Longo, A. Bertucco, I. Kikic, D. Solinas, Purification of artemisinin from hexane extracts of CIM-Arogya on solid matrix by supercritical CO_2, in: F. Cancell, J. Mercadier, J. Fages (Eds.), Proceedings of the 9th International Symposium on Supercritical Fluids ISSF, Arcachon (F), 2009, pp. 142–147.
[32] U. Salgin, N. Yildiz, F. Köroğlu, A. Çalimli, A parametric study of phenolic compounds desorption performance from organobentonite by supercritical fluids, J. Supercrit. Fluids 39 (2007) 296–303.
[33] M.D. Ruthven, Dynamics of adsorption columns: single transition systems, Principles of Adsorption and Adsorption Processes, Wiley-Interscience, New York, 1984, p. 227.