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Chapter 11

Carbon Dioxide Use in High-Pressure Extraction Processes

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Abstract

This chapter describes the use of carbon dioxide at high pressures as an alternative for the extraction of bioactive compounds in a more sustainable way, addressing some of its physicochemical properties, such as pressure, temperature, density, solvation, selectivity, and its interaction with the solute when modified by other solvents such as ethanol and water. This extraction process is considered chemically "green," when compared to conventional extraction processes using toxic organic solvents.

Keywords: supercritical CO_2, high pressure, density, vegetable matrix, bioactive compounds

1. Introduction

Separation technologies with fluids at high pressures are essentially vital to get new natural products of vegetable or marine origin that have biological activity, so-called bioactive extracts. Among the developed technologies, the supercritical fluid technology offers products free of residual solvent and that typically present high quality, when compared to products obtained by conventional techniques. The extracts of bioactive compounds can be obtained by extraction

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of solid matrices (leaves, seeds, pulps, etc.) or by extraction/fractionation of liquid mixtures (aqueous solutions, fish oils, microalgae oils, vegetable oil, deodorize distillates, etc.) [1–5]. In processes at high pressures, which are near or above the critical point (pressure and temperature), the solvent density increases drastically and this is the most important parameter associated to the solvent power. As illustrated in **Figure 1**, carbon dioxide, a non-toxic substance, acting as solvent, co-solvent, or anti-solvent, is the most important fluid used in the supercritical fluid technology in extraction, separation, fractionation, micronization, and encapsulation processes applied to obtain extracts concentrated with bioactive compounds for food, pharmaceutical, and cosmetic applications [6–9].

Carbon dioxide has a critical temperature near to room temperature, contributing to the operating conditions (pressure and temperature) to extract thermolabile substances, such as bioactive compounds. In addition, this substance is non-polar and to enlarge the application spectrum to extract bioactive compounds, ethanol, water, or both are usually used as co-solvents. Moreover, carbon dioxide acts as co-solvent when in the mixture it is used more than 60% of ethanol or water, and as anti-solvent, when the solute extract is not soluble in carbon dioxide during the depressurizing step.

The information accuracy related to the physical (pressure, temperature, and density) and transport properties (diffusivity, viscosity) and the accuracy of thermodynamic and mass transfer relations used for the solvent, co-solvent, and solute reach directly the costs of investment in extraction/separation units in supercritical conditions. The thermodynamic phase equilibrium determines the limits for the mass transfer among different phases, which are

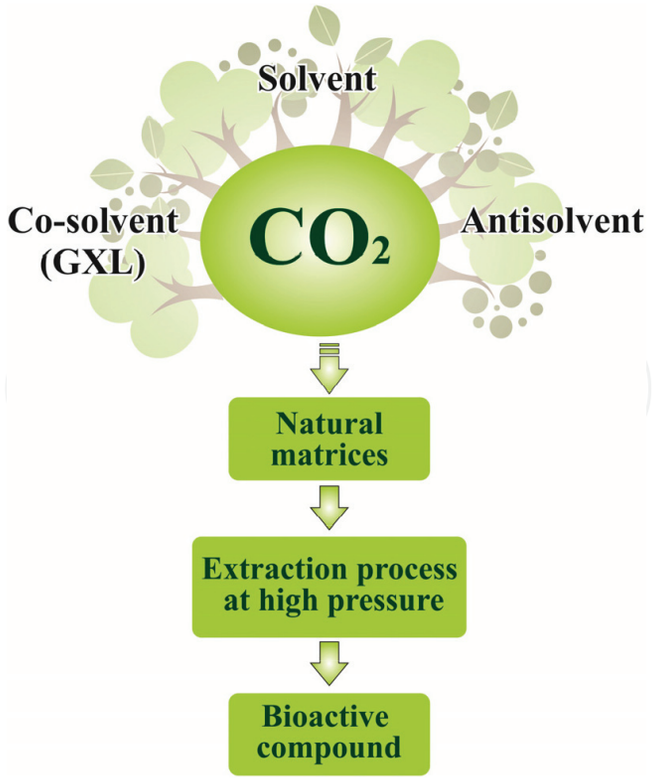


Figure 1. Carbon dioxide applications.

involved in various processes. The cubic equations of state are the most commonly applied models for the correlation and prediction of phase equilibrium at high pressures and are available in major commercial process simulators. In addition, they are used to calculate other thermodynamic properties, for both pure substances and mixtures, among which, the liquid and vapor phases density, enthalpy, and entropy.

This chapter intends to show the recent application scenarios of the carbon dioxide use at high pressures as solvent, to obtain natural extracts enriched with bioactive compounds, including the use of water as co-solvent to enhance the mixture solvating power. In this chapter, the description of the experimental strategy used for the supercritical carbon dioxide extraction of bioactive compounds from açaí berry pulp was emphasized. The primary properties of pure carbon dioxide were also described and calculated using equations of state.

2. Diagrams of pure substances

2.1. P-T diagram

The pressure versus temperature (P-T) diagram describes the different aggregation states of pure substances called solid, liquid, and vapor/gas.

Figure 2 is a schematic representation of the P-T diagrams for carbon dioxide and the substances most commonly employed as co-solvent, ethanol, and water, in high-pressure extraction processes

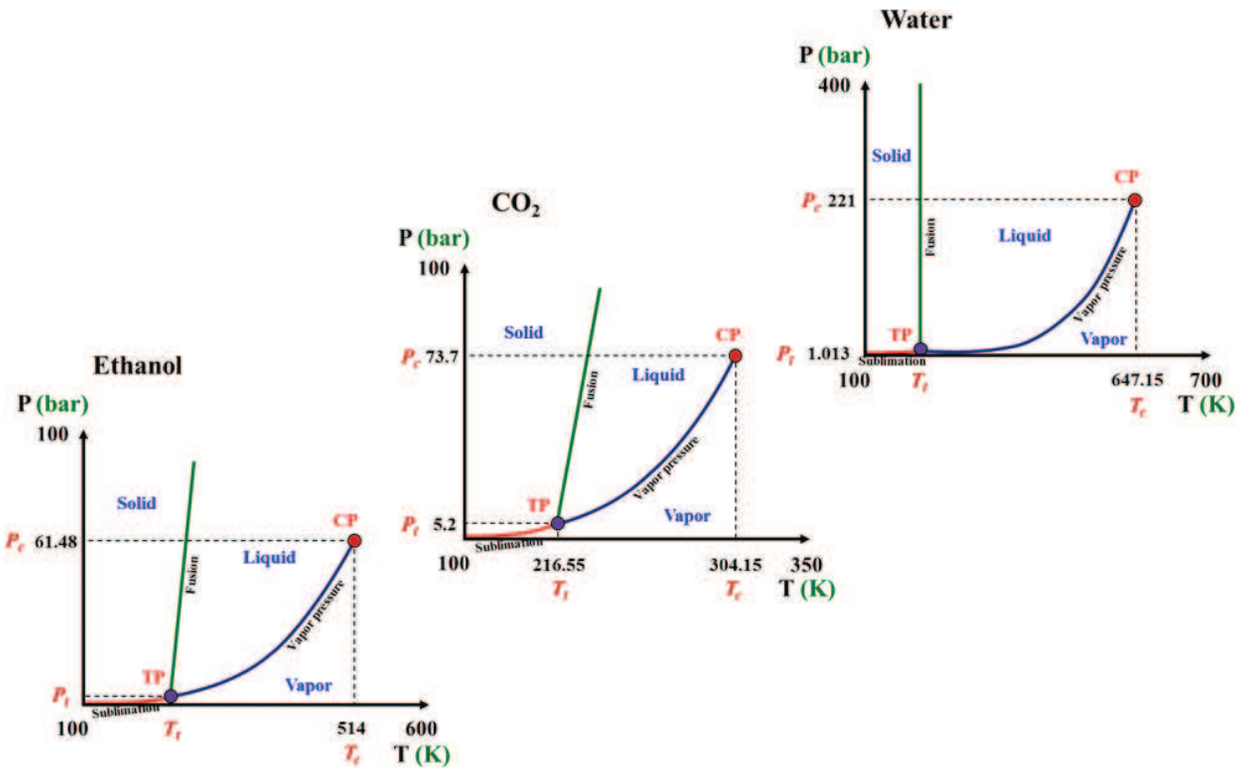


Figure 2. Solid-liquid-gas-supercritical fluid phase diagram. TP = triple point. C_P = critical point. P_c = critical pressure. T_c = critical temperature. T_t = triple point temperature. P_t = triple point pressure.

of bioactive compounds. The curves represent the boundaries (phase transition or phase equilibrium) between the different states, known as saturation curves. The curve between the solid and liquid phases is called fusion; the curve between solid and vapor phases is called sublimation and that one between liquid and vapor phases is called vapor pressure (also known as boiling curve).

The behavior of the thermodynamic diagrams of pure substances culminates in the determination of the reference equilibrium points that has great importance in the development of thermodynamic models for different processes applications. In the P-T diagram, there are two points: the triple point, where the three phases are in equilibrium and the critical point, which is particularly of fundamental interest for applications in processes that use solvents at high pressures.

The critical point of a pure substance is the maximum thermodynamic state reached by the saturation curve between liquid and vapor phases. When the substance is in the state above the critical temperature (T_c) and the critical pressure (P_c), it is called supercritical fluid, and when the pressure is above Pc and the temperature below Tc, the thermodynamic state is called subcritical liquid. The technology with fluids at high pressures consists in the use of substances that act like solvent when they are in the thermodynamic state near or above the critical point. The triple point of carbon dioxide is at pressure of 5.18 bar and at temperature of 216.58 K (−56.57°C), and the critical point is at pressure of 73.7 bar and at temperature of 304.15 K (31°C) [10].

2.2. P-ρ-T diagram

Density (ρ) is the most important thermodynamic property to define the solvating power of a solvent at high pressures, increasing the density of the solvent increases its solvating power. To better understand the influence of density on the solvating power to increase or decrease the solubility of an extract within a solvent at high pressures, one needs information concerning the density as a function of system pressure and temperature.

Figure 3 shows the schematic representation of the density behavior (ρ = 1/V) of a pure substance with temperature and pressure variations, where V is the specific volume (volume per mass unit). In **Figure 3**, the density versus pressure isotherms are presented in descending order from T1 to T9. The red line represents the saturation curve between the liquid and vapor phases. The highest point of the saturation curve is the critical point. The dotted line within the saturation curve is the two-phase region. In the saturation curve, there is a sudden difference in the density between the liquid and vapor phases.

The behavior of the P-ρ-T diagram shows that the density at constant temperature increases with the increasing pressure and at constant pressure increases with the decreasing temperature. In the region near the critical point, small variations of pressure and/or temperature cause great variations in density. For carbon dioxide, the critical point is at the pressure of 73.7 bar and at the temperature of 304.15 K (31°C); it makes carbon dioxide the most applied solvent to extract thermo-sensible substances.

Below the critical temperature, in the subcritical region, the isotherms present two types of behavior: for the vapor region, at constant pressure, the density increases with the decreasing temperature and for the liquid region, the density varies very little with the temperature.

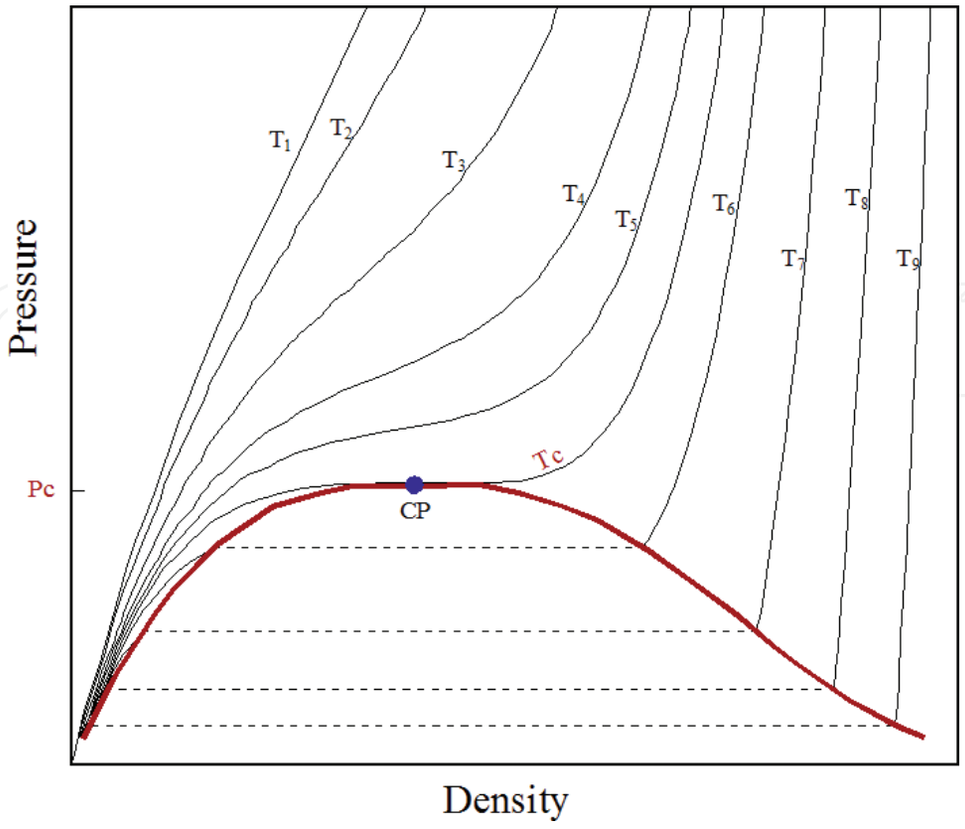


Figure 3. Pressure-density (P-ρ) phase diagram for carbon dioxide. CP = critical point (P_c, T_c, and ρ_c). CP = critical point (P_c, T_c, and ρ_c).

3. Supercritical fluid extraction

The extraction/separation processes applied to solid matrix using carbon dioxide as solvent are the most studied supercritical processes in the search for new natural products that have biological activity, according to numerous applications described in the literature [1, 4–6, 11–18].

3.1. General process steps

Generally, the supercritical fluid extraction applied to a natural solid matrix consists of three steps: the system supply of solvent/co-solvent, the extraction unit, and the extract separation system from solvent/co-solvent. **Figure 4** presents a general scheme of the supercritical fluid extraction unit without solvent recycle. The system supply of solvent/co-solvent consists by a booster air-driven fluid pump, a cooling bath, a co-solvent recipient, a co-solvent pump, and a mixer. The extract separation system from solvent/co-solvent consists by a control valve for extraction pressure reduction and a separation vessel to collect the extract.

Regarding the extraction, the supercritical solvent continuously flows through a fixed bed of solid particles and dissolves the extractable components of the solid. The solvent is fed into the extractor and evenly distributed at the inlet of the fixed bed. The system solvent and soluble components leave the extractor and feed the precipitator/separator, where the solvent products

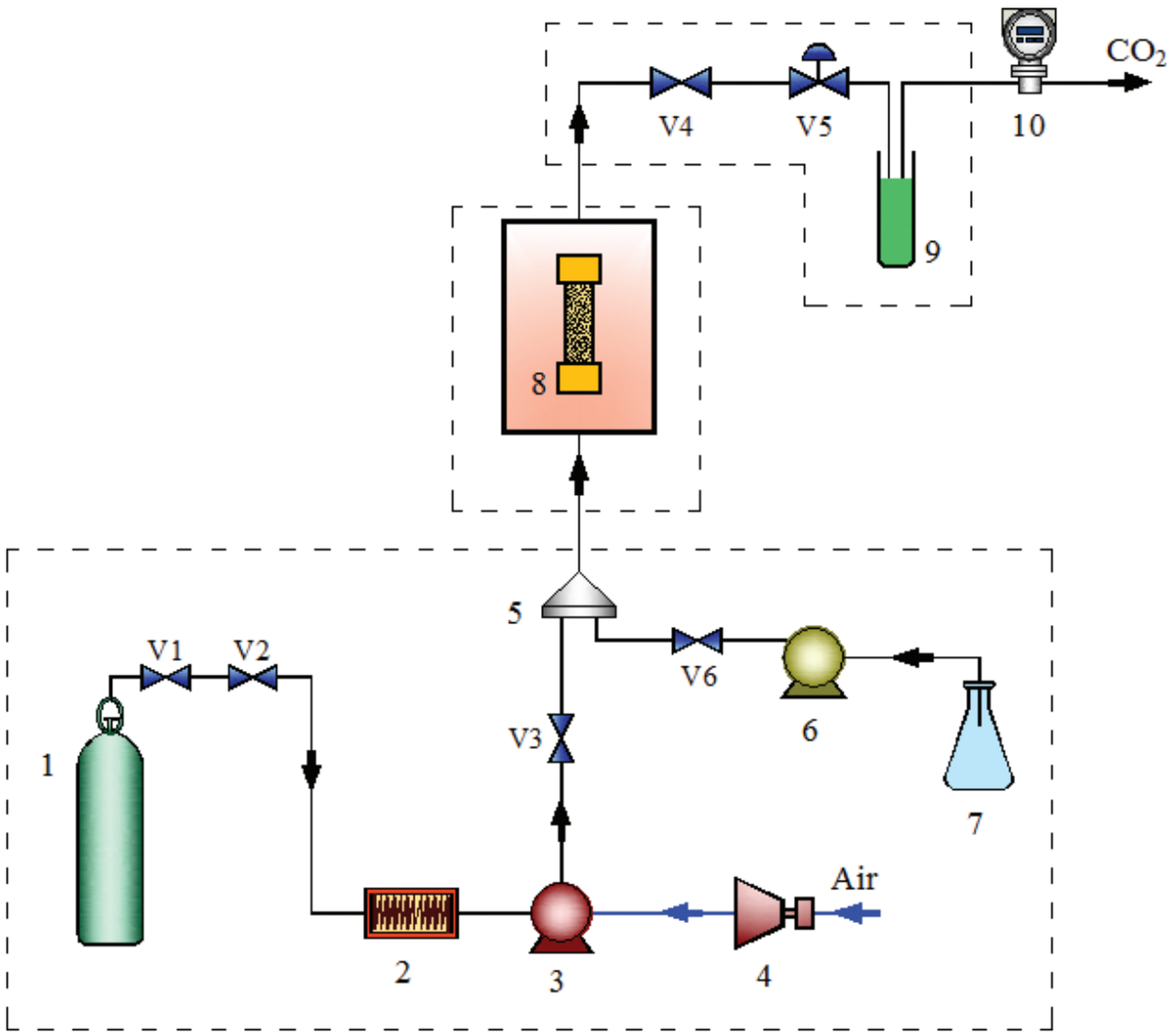


Figure 4. Scheme of a supercritical fluid extraction plant applying solvent/co-solvent. CO_2 cylinder (1); cooling bath (2); booster (CO_2 pump-3 and Compressor-4); mixer (5); CO-solvent pump (6); co-solvent recipient (7); extraction unit (8); control valve (V-5); separation vessel (9); flow meter (10).

are separated by expansion (depressurizing), since at low pressures the density of the solvent sharply decreases, therefore it decreases the solubilizing power of the solvent as well and the products precipitate.

The choice of the operating condition (P and T) is a determining factor that contributes to the maximization of the extracts solubility in the supercritical solvent, and consequently the extraction yields. Thus, increasing the density of the supercritical fluid, the solubility of the solvent maximizes. The solubility increasing can also occur when a co-solvent is added, which changes the solvent power and, in this way, the new solvent is a mixture [19, 20].

To design a high-pressure fluid extraction process of valuable compounds from new natural solid matrices, it is necessary to define the size of the extraction unit and some important parameters have to be determined to obtain the optimum process conditions for each application. Brunner

[19] and Kiran et al. [21] described the most important parameters, and among the variables that determine the process, operating conditions (pressure and temperature), amount of solvent, conditions of solvent removal from extract (precipitation), pretreatment of solid matrix, and other mass transfer parameters can be highlighted.

In general, the parameters that define the behavior of the mass transfer at processes at high pressures are related to the configuration of the bed: particle size, height, and diameter, preparation of the raw material, solvent flow, among others, which contribute to define the shape of the kinetic extraction curves. The phenomenological discussions about supercritical fluid extraction mass transfer applied to solid matrices have been discussed in the literature [19, 22–24].

3.2. Supercritical carbon dioxide extraction of bioactive compounds: a case study

The experimental strategy used for the supercritical carbon dioxide extraction process of bioactive compounds is based on the previous results collected by our research group in obtaining açai extracts [25].

Açaí is a dark purple, berry-like fruit from typical Amazon palm tree *Euterpe oleracea* Mart., integrated in the daily dietary habit of the native people.

Recently, many studies have suggested its use as a functional food or food ingredient due to its antioxidant activity, explained by the high content of phenolic compounds, such as anthocyanins, specially cyanidin-3-glucoside and cyanidin-3-rutinoside, flavones, and phenolic acids [26–28]. Phenolic constituents are generally associated with health-promoting properties and prevention of diseases [29–33]. Anthocyanins constitute a group of pigments, also important in the food industry, for the replacement of artificial colors [34–36].

The supercritical extraction experiments of the lyophilized açaí pulp under development were carried out in a Spe-ed™ SFE commercial unit (Allentown, PA, USA: model 7071 from Applied Separations) which is coupled to the solvent + co-solvent delivery system of Laboratory of Supercritical Extraction (LABEX), Faculty of Food Engineering-UFPA. The schematic representation of the supercritical extraction system is shown in **Figure 5**.

The first step consisted of the extraction with supercritical CO_2 (pure) to obtain extracts rich in fatty acids and byproducts of the residual solid matrix (defatted pulp). Analyses of the content of bioactive compounds (anthocyanins and total phenolic compounds) were performed. The second stage that is under development consists of the extraction with supercritical CO_2 combined with water as co-solvent applied to the residual solid matrix to obtain extracts concentrated in anthocyanins.

In the first stage, Batista et al. [25] subjected samples of lyophilized açaí pulp to the supercritical carbon dioxide extraction process. Among the results, the study of the process variables (temperature, pressure, and solvent density) that maximize the extraction yield of açaí oil, the quantification of the total anthocyanins content and total phenolic compounds content, and the evaluation of the allelopathic potential of the extracts obtained can be highlighted.

Figure 6 shows the experimental results of the 50, 60, and 70°C isotherms on dry basis and their standard deviations. In this study, the highest global yield was equal to 45.4 ± 0.58%,

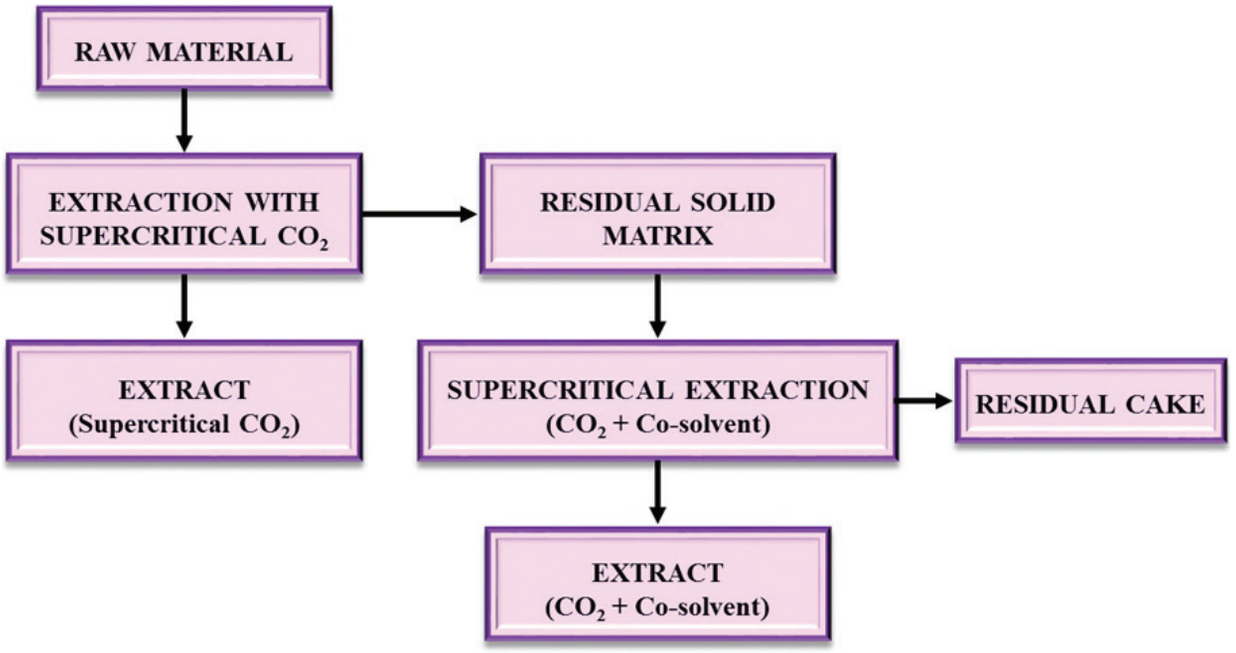


Figure 5. Experimental protocol for the bioactive compounds extraction.

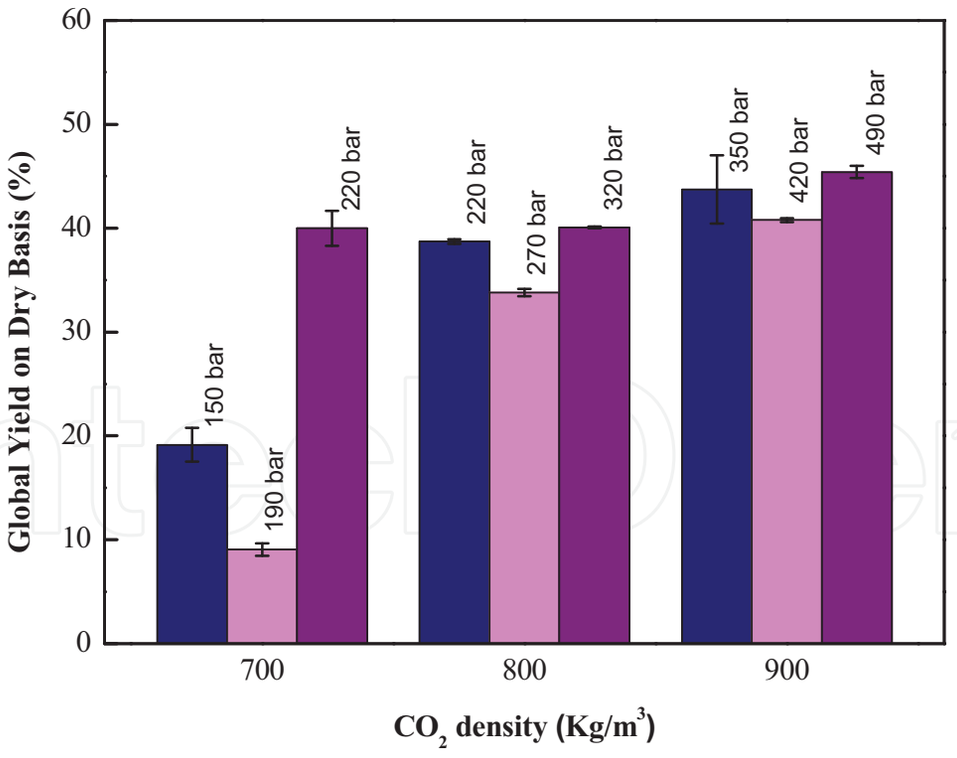


Figure 6. Global yield on dry basis versus density of supercritical CO_2 extraction of lyophilized açaí berry oil. (■) 50°C, (■) 60°C, and (■) 70°C isotherms [17].

obtained at 70°C and 490 bar, while the lowest global yield was equal to 9.07 ± 0.6%, obtained at 60°C and 190 bar. The density is related to the CO_2 solubility and is directly influenced by temperature and pressure. Here, the most important parameter was the density, since when it increased (in all isotherms), the oil global yield also increased.

The analysis of the phenolic compounds in the lyophilized açaí berry pulp showed an increase in its content comparing the samples before and after the extraction with supercritical CO_2, in different conditions. Its highest content was equal to 7565 mg/100 g and was obtained in the condition of 70°C and 350 bar. The standard deviation for each condition was lower than 0.18% (**Figure 7**). Regarding anthocyanins, there was also an increase in its content. Before the extraction with supercritical CO_2, the total concentration was equal to 96.58 ± 0.11 mg/100 g, and after the extraction, it reached up to 137.5 mg/100 g of sample in the condition of 50°C and 220 bar. The standard deviation was lower than 0.15%. **Figure 8** shows the values obtained and their specific deviation. It can be inferred that since the extracts of the lyophilized acaí berry pulp obtained by supercritical CO_2 are rich in phenolic compounds and anthocyanins, it presents great potential in nutraceutical applications.

The results of the fatty acid profile analysis of açaí extracts indicate a low saturated/unsaturated ratio except for the condition of 70°C and 320 bar. The SFA content reached 99.67% at the condition of 70°C and 320 bar.

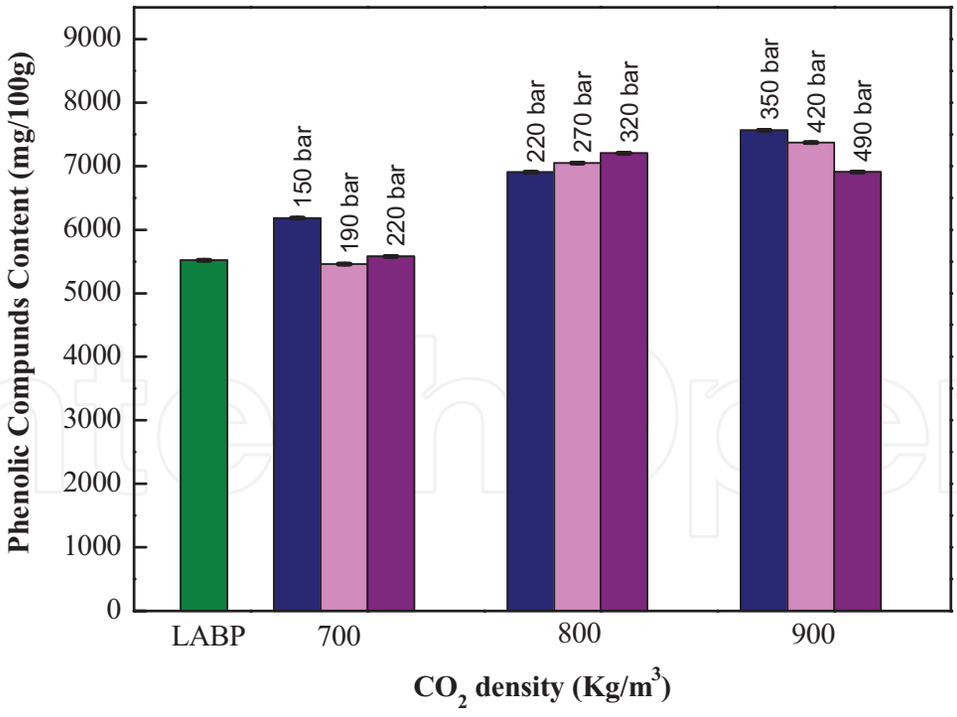


Figure 7. Total phenolic compounds content in lyophilized açaí berry pulp before and after extraction with supercritical CO_2. (■) 50°C, (■) 60°C, and (■) 70°C isotherms [17].

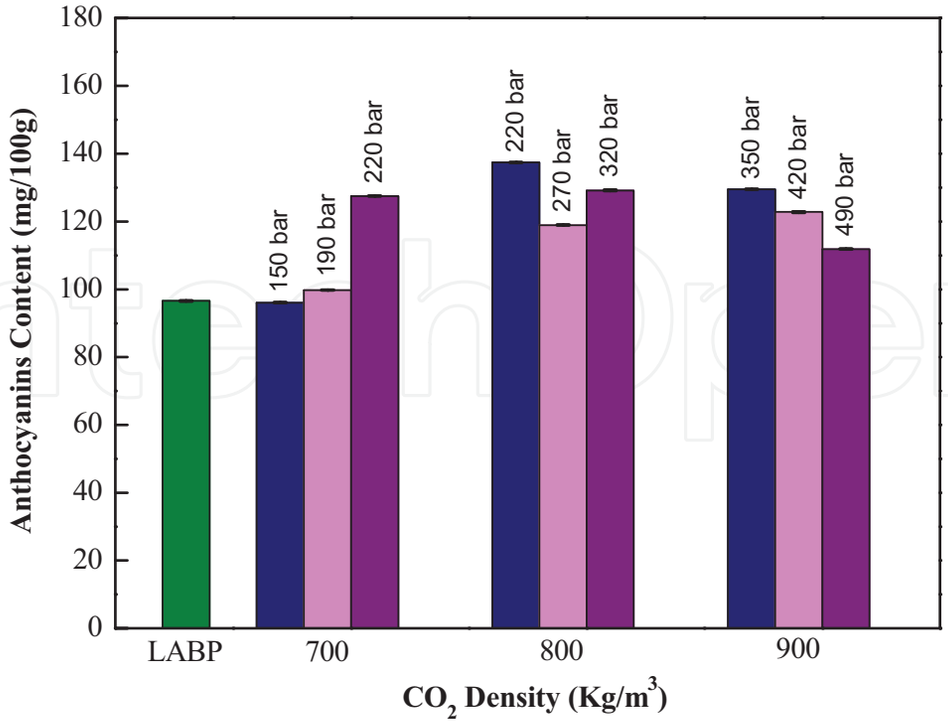


Figure 8. Total anthocyanins compounds content in lyophilized açaí berry pulp before and after extraction with supercritical CO_2. (■) 50°C, (■) 60°C, and (■) 70°C isotherms [17].

4. High-pressure carbon dioxide properties

4.1. Thermodynamic properties

The influence of the density in the solvation power by the tunable operating conditions (P, T) is the most important thermodynamic effect in the high-pressure fluid processes.

Above the critical point, the supercritical extraction process can operate over a wide range of operating conditions (P, T) and the simplest density behavior can be obtained through an isotherm, being possible to select a wide range of operating pressures, as shown in **Figure 3** of the item 2.2 for the isotherms T1 > T2 > T3 > T4 > T5.

The density is defined by the inverse of specific volume, and for practical purpose, could be calculated by volumetric properties (P-V-T) using equation of state.

4.1.1. P-V-T diagram calculation with equations of state

To describe the P-V-T diagram behavior, it is necessary to use precise equations of state (EOS) with specific parameters for pure substances. In the case of carbon dioxide, the equations of Bender [19] and Span and Wagner [37] are the most used. The Bender equation is presented below, where the parameters were determined from experimental PVT data of carbon dioxide. **Table 1** shows the parameters of the Bender equation.

i	a_i	i	a_i
1	0.22488558	11	0.12115286
2	0.13717965×10^{3}	12	$0.10783386 \times 10^{-3}$
3	0.14430214×10^{5}	13	$0.43962336 \times 10^{-2}$
4	0.29630491×10^{7}	14	$-0.36505545 \times 10^{8}$
5	0.20606039×10^{9}	15	$0.19490511 \times 10^{11}$
6	$0.45554393 \times 10^{-1}$	16	$-0.29186718 \times 10^{13}$
7	$0.77042840 \times 10^{-2}$	17	0.24358627×10^{8}
8	0.40602371×10^{5}	18	$-0.37546530 \times 10^{11}$
9	0.40029509	19	$0.11898141 \times 10^{14}$
10	$-0.39436077 \times 10^{-3}$	20	0.50000000×10^{1}

Table 1. Bender equation constants for CO_2 [19].

$$P = \frac{T}{V}\left[R + \frac{B}{V} + \frac{C}{V^2} + \frac{D}{V^3} + \frac{E}{V^4} + \frac{F}{V^5} + \left(G + \frac{H}{V^2}\right)\frac{1}{V^2}\exp\left(-a_{20}/\ V^2\right)\right] \tag{1}$$

where

$$B = a_1 - \frac{a_2}{T} - \frac{a_3}{T^2} - \frac{a_4}{T^3} - \frac{a_5}{T^4} \tag{2}$$

$$C = a_6 + \frac{a_7}{T} + \frac{a_8}{T^2} \tag{3}$$

$$D = a_9 + \frac{a_{10}}{T} \tag{4}$$

$$E = a_{11} + \frac{a_{12}}{T} \tag{5}$$

$$F = \frac{a_{13}}{T} \tag{6}$$

$$G = \frac{a_{14}}{T^3} + \frac{a_{15}}{T^4} + \frac{a_{16}}{T^5} \tag{7}$$

$$H = \frac{a_{17}}{T^3} + \frac{a_{18}}{T^4} + \frac{a_{19}}{T^5} \tag{8}$$

$$a_{20} \approx V_C^2 \tag{9}$$

Figure 9 shows the calculation with Bender equation [19] of state for the P-V-T diagram isotherms and saturation curve, including an isotherm close to the critical temperature of the carbon dioxide. The calculations were performed using a Microsoft Excel spreadsheet. The equation presents accuracy in calculations when compared to data taken from IUPAC International Thermodynamic Table.

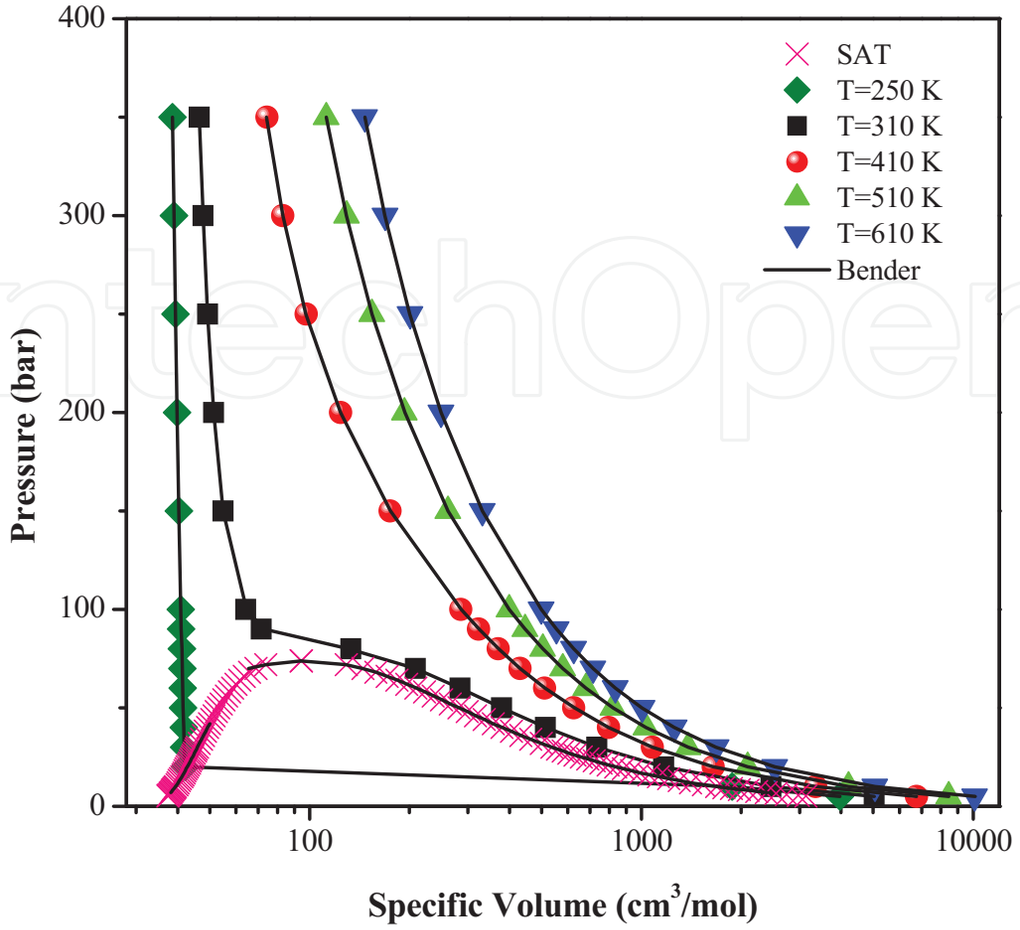


Figure 9. P-V-T diagram of carbon dioxide calculated with Bender EOS and compared to IUPAC data (symbols).

However, for applications of supercritical technology, it is necessary to calculate other thermodynamic properties. The thermodynamic properties of the pure solvent (density, enthalpy, and entropy) and the thermodynamic properties of the solute/solvent mixture, among which the equilibrium compositions, enthalpies, and mixing entropies, must be calculated in the operating conditions throughout the process. The cubic equation of state, also called Van der Waals type equation, represents an alternative, since the Bender-type equation described above is complex. In these cases, the cubic equations of state of Peng-Robinson (PR) [38] and Soave Redlich-Kwong (SRK) [39] are presented as the most commonly applied options in process simulations (**Table 2**). These equations of state use various thermodynamic properties and the following physical properties of the pure substance: critical pressure, critical temperature, and the acentric factor, which are tabulated, in the case of carbon dioxide.

Table 3 shows the calculated values of the carbon dioxide densities for some isotherms above the critical point using the equations of Peng-Robinson [38] and Soave-Redlich-Kwong [39]. The computational package PE 2000 developed by Pfohl et al. [40] was used for calculations. The results are compared to data taken from IUPAC International Thermodynamic Table and from NIST Chemistry Webbook (NIST Standard Reference Database). The Peng-Robinson equation of state presented the best results for the carbon dioxide density calculation in the conditions of pressure and temperature of **Table 3** when compared with different databases.

Cubic equations			
PR	$P = \frac{RT}{V-b} - \frac{a(T)}{V(V+b)+b(V-b)}$	$a = 0.45724\ \frac{R^2T_c^2}{P_c} \times \alpha(T_r,\omega)$	$b = 0.07780\frac{RT_c}{P_c}$
		$\alpha(T_r,\omega) = \{1 + km[1-(T_r)^{1/2}]\}^2$	
		$km = 0.37464 + 1.54226\omega - 0.26992\omega^2$	
SRK	$P = \frac{RT}{V-b} - \frac{a(T)}{V(V+b)}$	$a = 0.42748\frac{R^2T_c^2}{P_c} \times \alpha(T_r,\omega)$	$b = 0.08664\frac{RT_c}{P_c}$
		$\alpha(T_r,\omega) = \{1 + km[1-(T_r)^{1/2}]\}^2$	
		$km = 0.480 + 1.574\omega - 0.176\omega^2$	

Table 2. Cubic equations of state.

Pressure (bar)	Temperature (°C/K)	CO_2 density (kg/m^3)			
		PR	SRK	NIST	IUPAC
100	36.85/310	617.3	563.0	683.4	686.5
200		847.8	763.8	855.5	857.0
300		941.1	846.6	921.5	922.7
100	46.85/320	418.1	390.6	444.6	449.4
200		781.5	707.9	801.5	803.1
250		845.3	763.8	848.0	849.5
300		893.0	805.9	882.4	883.7
400		963.2	868.2	933.2	934.4
100	66.85/340	260.5	246.2	258.1	258.6
200		643.2	589.3	678.7	680.5
250		731.7	666.7	751.9	753.3
300		794.4	721.8	800.6	801.8
400		882.9	799.6	866.7	867.9

Table 3. Carbon dioxide density calculated with different equations of state.

Figure 10 shows the calculation with Peng-Robinson [38] equation of state for P-V-T diagram isotherms and saturation curve, including an isotherm close to the critical temperature of the carbon dioxide. The Peng-Robinson equation of state was able to describe all the phases of the carbon dioxide P-V-T diagram for the isotherms studied when compared to data taken from IUPAC International Thermodynamic Table.

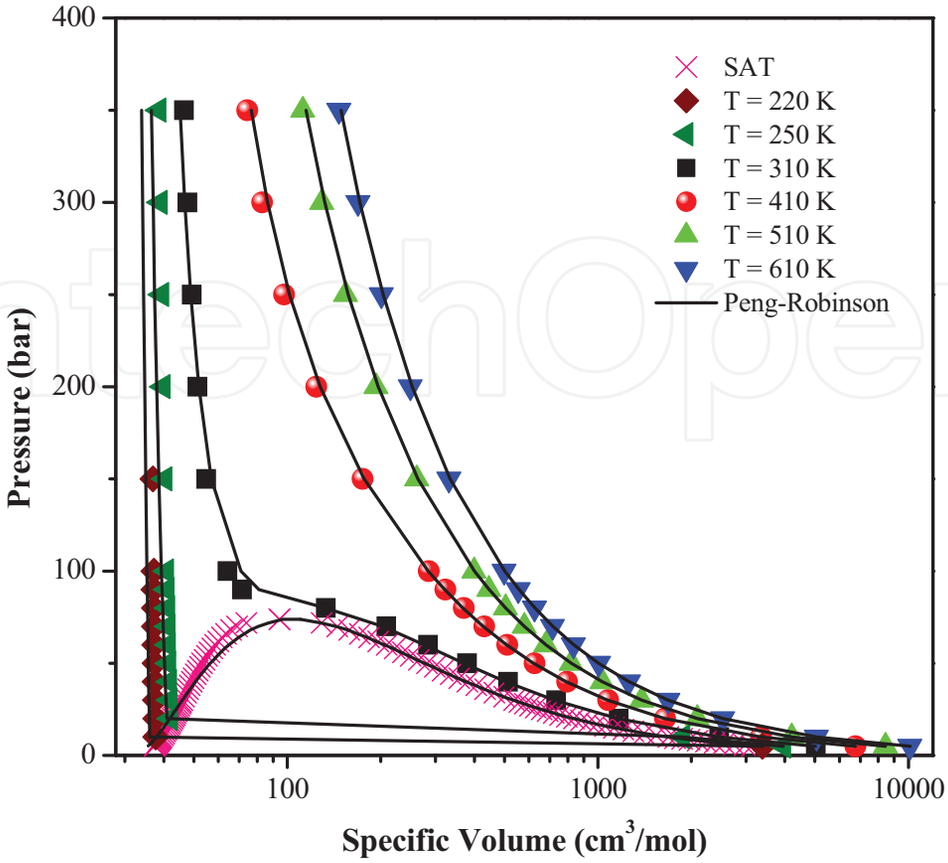


Figure 10. PVT diagram of carbon dioxide calculated with Peng-Robinson EOS and compared to IUPAC data (symbols).

From a process point of view, the accuracy of the cubic equations of state was good, considering that the operating conditions commonly applied in CO_2 extraction at high pressures are close to the values of temperature and pressure used in **Table 3**.

4.2. Other high-pressure carbon dioxide properties

The application of the high-pressure fluid extraction technologies in both laboratory and industrial scales requires not only the knowledge of the physical and thermodynamic properties of the solvent, but also requires the understanding of thermal and transport properties behavior. Among them, the most commonly cited are viscosity, diffusivity, thermal conductivity, and dielectric constant.

The dielectric constant describes the ability of a solvent to be polarized. The dielectric constant value is associated with the ability to dissolve electrolytes or polar compounds. The dielectric constant increases with temperature for most substances [41]. The dielectric constant of supercritical carbon dioxide with approximate value of a hydrocarbon alone does not characterize it as an important solvent; it only identifies it as a non-polar substance. Its solvation power is mainly related to the considerable increase of its density in the supercritical region with the properties as viscosity and diffusivity complementing the characteristics that makes supercritical carbon dioxide a differentiated solvent.

Under supercritical conditions, the thermal conductivity is influenced by both temperature and pressure and at constant pressure this property increases with increasing temperature, and on the other hand, at constant temperature, the thermal conductivity increases with pressure [42].

Carbon dioxide and other supercritical solvents have low viscosity and high diffusivity values. The viscosity and thermal conductivity of gases and liquids differ by one to two orders of magnitude, and the diffusivity values of gases and liquids differ by four orders of magnitude [41].

In the supercritical state, the substances have intermediate characteristics between the properties of a gas and a liquid, which contributes to more favorable hydrodynamic properties than the liquids, with diffusion coefficients close to those of a gas, which provides a fast and efficient mass transfer. Another feature of the supercritical fluid includes its low viscosity, which facilitates the penetration of the fluids into a solid matrix. Therefore, high diffusivity and low viscosity lead to a faster extraction time providing a dissolving power so that the supercritical fluid is considered a solvent.

Table 4 shows that supercritical fluids are characterized by transport properties (viscosity and diffusivity) between gases and liquids. The viscosity of a supercritical fluid is smaller than the viscosity of a gas and the diffusivity of the liquid is greater than the diffusivity of a supercritical fluid. In summary, the scheme of **Figure 11** shows the basic properties of supercritical carbon dioxide, which become fundamental in high pressures extraction processes.

	Unit	Gas	SCF	Liquid
Viscosity	Pa s	10^{-5}	10^{-4} to 10^{-5}	10^{-3}
Diffusivity	cm^2/s	10^{-1}	10^{-3} to 10^{-4}	10^{-6}

Table 4. Order of magnitude of transport properties.

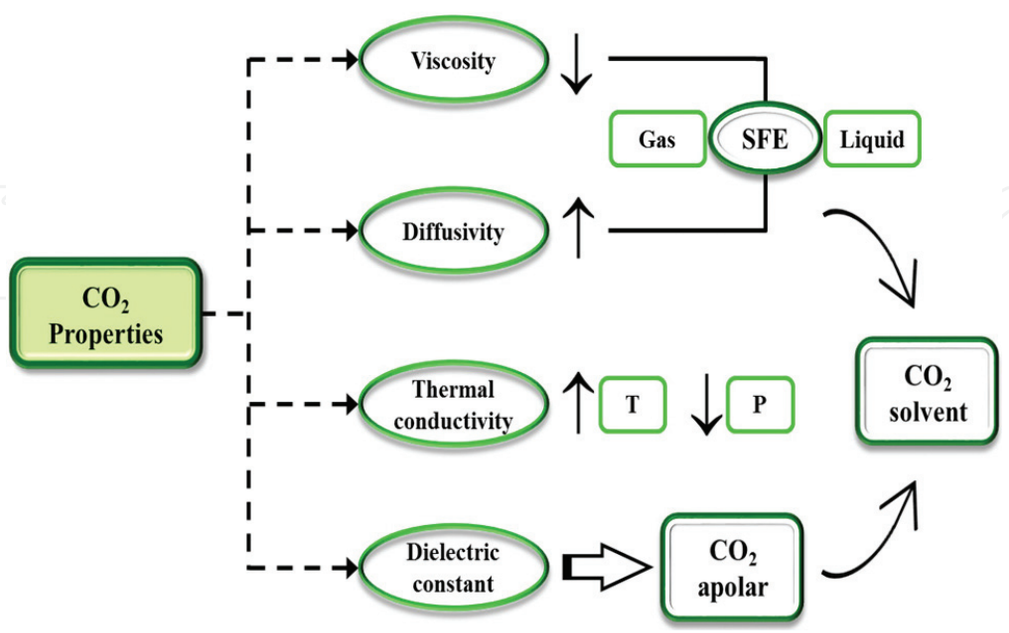


Figure 11. Carbon dioxide properties.

5. High-pressure carbon dioxide applications

The most cited drawback of using supercritical carbon dioxide as solvent is the high investment cost for equipment acquisition and operation. However, the extraction with supercritical carbon dioxide presents a lower extraction time because of its diffusivity and low surface tension, greater selectivity in the compounds of interest and little or no consumption of organic solvents [43–46].

5.1. Essential oil extraction

Essential oils have been used to prevent or treat human diseases for several centuries. The extraction of the volatile compounds present in edible or medicinal aromatic plants is generally carried out by hydrodistillation; however, the authors report that some compounds may undergo hydrolysis during the extraction period [47]. Although there are other techniques for isolating essential oils, the use of CO_2 as supercritical fluid has been considered a "chemically green" unconventional extraction technique that does not alter or degrade the substances present in oils because it uses relatively low temperatures in the extraction process.

Guan et al. [48] performed a comparison between conventional extraction methods and extraction with supercritical CO_2 and observed that the extraction using supercritical CO_2 as solvent was less effective with recovery rate of 57.36% for eugenol compared to steam distillation with 58.2%, but it was more effective when compared to hydrodistillation with recovery rate of 48.82% and Soxhlet extraction with 57.24%. However, when compared with the extraction of eugenol acetate, the extraction with supercritical CO_2 presented higher yields in relation to the other extraction methods.

Extraction of chemically active volatile molecules with supercritical CO_2 is very widespread [49–51]. This is due to the possible applications as agents that promote biological activities [52], such as antioxidant activity [53], anti-inflammatory activity [54], insecticidal activity [55], and phytotoxic activity [56]. In **Table 5**, some studies in the literature on the extraction of essential oils with supercritical CO_2 can be observed.

Aromatic plant	Bioactive compounds	References
Juniperus communis L.	Germacrene D and 1-octadecene.	[57]
Satureja hortensis	γ-Terpinene, thymol, and carvacrol	[58]
Myrtus communis L.	Methyl eugenol, 1,8 cineole, and beta- caryophyllene	[59]
Leptocarpha rivularis	α-thujone, β-caryophyllene, and caryophyllene oxide	[60]
Piper nigrum L.	β-caryophyllene, limonene, sabinene, 3-carene, β-pinene, and α-pinene	[53]
Camellia sinensis L.	9-Thiabicyclo[3.3.1]non-7-en-2-ol, tricosane, heneicosane, tetracosane, and dibutyl phthalate	[61]

Table 5. Published studies on extraction of essential oils using CO_2 as supercritical fluid.

As given above, it is observed that the process of extraction of essential oils using supercritical CO_2 is ecologically a cleaner method than the conventional ones, and it has been seen as one of the most viable alternatives.

5.2. Phytosterols extraction

Phytosterols (plant sterols) are non-volatile triterpenes. The great majority of these compounds are formed by carbon with one or two carbon-carbon double bonds [62]. And the most common phytosterols found in plants are β-sitosterol, campesterol, and stigmasterol [63]. These compounds have various biological activities such as lowering the total serum or plasma cholesterol levels and the low-density lipoprotein cholesterol levels. In addition, they have antitumor activities inhibiting the development of colon cancer [64, 65].

For the extraction of these phytosterols, the supercritical CO_2 has been shown to be an efficient technique for extraction of fixed oils from vegetable matrices. Studies report that this solvent may be superior to obtain oils in relation to the conventional extraction, exhibiting a recovery rate of phytosterols of 836.5 mg/100 g versus 30.5/100 g using a Soxhlet-type extraction apparatus [66]. A very important parameter for the extraction of phytosterols with supercritical CO_2 is the increase of the pressure, because it favors the solvation power and consequently the solubilization of these compounds, with a recovery rate of up to 7262.80 $mg.kg^{-1}$ [67]. **Table 6** presents some articles published in the literature on the extraction of phytosterols using supercritical CO_2.

5.3. Carotenoid extraction

Carotenoids are tetraterpenes present in plants that have several applications in food [72], cosmetic [73], and pharmaceutical [74] areas. Some of the benefits provided by these pigments are: antioxidant activity and strengthening of the immune system against degenerative diseases such as cancer, cardiovascular diseases, muscle degeneration, inflammation, hypertension, insulin resistance and obesity [75, 76].

Because of their hydrophobic characteristics, carotenoids are usually extracted using organic solvents such as hexane and petroleum ether. Carotenoids with hydrophilic characteristics can be obtained with more polar solvents such as acetone, ethanol, and ethyl acetate [77]. The

Plants	Phytosterols	References
Cucurbita pepo convar	Desmosterol, campesterol, stigmasterol, β-sitosterol, spinasterol, Δ7,22,25-stigmastatrienol, Δ7-stigmastenol, Δ7,25-stigmastadienol, and Δ7-avenasterol	[68]
Brassica napus	β-sitosterol, campesterol and brassicasterol	[69]
Hippophae rhamnoides L.	β-sitosterol	[70]
Sesamum indicum L.	β-sitosterol + sitostanol, cholesterol, campesterol + campestanol +24-methylene cholesterol, Δ-5 avenasterol and stigmasterol, while lower levels of Δ-5,24 stigmastadienol, brassicasterol, clerosterol + Δ-5-23 stigmastadienol, Δ-7 avenasterol, eritrodiol and Δ-7 stigmasterol	[71]

Table 6. Phytosterols extracted using supercritical CO_2

techniques used to extract this compound may be maceration, Soxhlet, microwave-assisted extraction [78, 79], ultrasound-assisted extraction [80], pressurized liquid extraction [81, 82], and supercritical fluid technology using low temperature. The process is performed in a short time in relation to conventional processes and does not use toxic solvents to collect the compound of interest [83]. In **Table 7**, some published works that used supercritical CO_2 to obtain carotenoids are shown.

5.4. Fatty acids extraction

Fatty acids (FA) belong to the lipid class and differ according to the size of the C chain (2–80), the presence or absence of double bonds (saturated or unsaturated) or their radical function as the groups hydroxyl, epoxy, and halogen atoms [89]. Ingestion of FA is essential to have an adequate energy balance in the human organism in addition to reducing the risk of some diseases such as diabetes [90], hypertension [91], coronary diseases [92], and inflammation [93].

Some of its applications are in food, nutraceutical, and cosmetic industries, and in the production of lubricants, biodiesel, and glycerol [94–96]. Some of the extraction methods that can be used to obtain FA are mechanical extraction [97], extraction by supercritical fluids and organic solvent [98], microwave-assisted extraction [99], and supercritical CO_2 extraction [98]. **Table 8** shows some studies that used supercritical CO_2 to obtain the main classes of the FA group.

5.5. Extraction with supercritical CO_2 modified with ethanol/water

The extraction with supercritical CO_2 modified with water in different proportions is carried out to obtain bioactive compounds of high polarity, because as mentioned above, CO_2 is an

Raw material	Carotenoid	References
Tomato juice	Lycopene and β-carotene	[84]
Hemerocallis disticha	Lutein and zeaxanthin	[85]
Dunaliella salina	9-cis and trans-β-carotenes	[86]
Undaria pinnatifida, *Haematococcus pluvialis*, and *Chlorella vulgaris*	Fucoxanthin, astaxanthin, lutein, and β-carotene	[87]
Fucus serratus and *Laminaria digitata*	Xanthophyll and fucoxanthin	[88]

Table 7. Published studies about carotenoid extraction using CO_2

Raw material	Fatty acid	Reference
Cucurbita ficifolia, Bouché	ω6-linoleic acid, palmitic acid, oleic acid	[100]
Farfantepenaeus paulensis	Palmitic acid, oleic acid, stearic acid, palmitoleic acid, and linoleic acid	[101]
Cannabis sativa L.	Linoleic acid and linolenic acid	[102]
Chaetoceros muelleri	Myristic acid, palmitic acid, and palmitoleic acid	[103]
Saw Palmetto	Lauric acid, mystiric acid, and oleic acid	[104]

Table 8. Published studies about fatty acids extraction using CO_2

Raw material	Compounds	References
Myrciaria cauliflora	Anthocyanin	[8]
Elderberry (*Sambucus nigra*)	Anthocyanins	[110]
Vitis vinifera var. Malvasia nera	Anthocyanins	[111]
Arrabidaea chica	Anthocyanins and luteolin	[112]
Scutellaria lateriflora L.	Baicalin, dihydrobaicalin, lateriflorin, ikonnikoside I, scutellarin, oroxylin A 7-O-glucuronide, oroxylin A, baicalein, wogonin	[113]
Vaccinium myrtillus L.	Delphinidin 3-O-galactoside, delphinidin 3-O-glucoside, cyanidin 3-O-galactoside, delphinidin 3-O-arabinoside, cyanidin 3-O-glucoside, petunidin 3-O-galactoside, cyanidin 3-O-arabinoside, petunidin 3-O-glucoside, peonidin 3-O-galactoside, petunidin 3-O-arabinoside, peonidin 3-O-glucoside, malvidin 3-O-galactoside, peonidin 3-O-arabinoside, malvidin 3-O-glucoside, malvidin 3-O-arabinoside and malvidin 3-O-xyloside	[114]

Table 9. Phenolic compounds extracted with supercritical CO_2 modified with ethanol/water.

non-polar molecule and does not have "power" to solubilizate polar substances as is the case of the phenolic compounds (phenolic acids and flavonoids) [105, 106]. As previously mentioned, parameters of processes, such as temperature and pressure, can influence the extraction of bioactive compounds. Besides these two parameters, anthocyanins are also important for the extraction of phenolic compounds. Solvent flow rate, percentage of co-solvent, co-solvent type (ethanol or water), and extraction time are parameters that directly implicate the yield of these substances at the end of the extraction process [107].

Further examples of extraction of phenolic compounds using supercritical CO_2 modified with co-solvents can be analyzed in the studies [106, 108, 109]. They extracted various flavonoids like quercetin, catechin, epicatechin from cranberry, blueberry, and raspberry. **Table 9** presents some studies in which supercritical CO_2 modified with ethanol/water were used to extract chemically active phenolic compounds.

6. Conclusion

Carbon dioxide can be safely applied in high-pressure extraction processes due to its numerous advantageous characteristics. It is neither toxic nor inflammable, being able to act as solvent, co-solvent, or anti-solvent, which allows it to be used in natural products and foodstuff processing that require treatments intending to preserve their nutritional and sensory properties. Since it is a non-polar substance, it is suitable for extraction of non-polar bioactive compounds when used in pure form. When associated with a polar co-solvent, it can be used for extraction of polar compounds such as phenolic compounds and anthocyanins. Therefore, these characteristics make carbon dioxide the most important fluid used in high-pressure processes for extraction, separation, fractionation, micronization, and encapsulation, applied to obtain concentrated extracts with bioactive compounds for food, pharmaceutical, and cosmetic applications.

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