Gavin Publishers
Food & Nutrition Journal
Volume 1; Issue 02
Bimakr M and Ganjloo A.
ISSN: 2575-7091

Review Article

Supercritical Carbon Dioxide Extraction of Bioactive Compounds

MandanaBimakr*, Ali Ganjloo
Department of Food Science and Technology, University of Zanjan, Zanjan, Iran

***Corresponding author:** Bimakr M, Department of Food Science and Technology, Faculty of Agriculture, University of Zanjan, Zanjan, Iran, E-mail: mandanabimakr@yahoo.com

Citation: Bimakr M and Ganjloo A (2016) Supercritical Carbon Dioxide Extraction of Bioactive Compounds. Food Nutr J 1: 110. DOI: 10.29011/2575-7091.100010

Received: 01 September, 2016; **Accepted:** 01 October, 2016; **Published:** 07 October, 2016

Abstract

The application of Supercritical Fluid Extraction (SFE) on the valuable bioactive compounds recovery from plant matrices has several advantages as compared to the conventional organic solvent extraction methods, especially for environmental considerations. In recent years, SFE has been received as a clean and environmentally friendly "green" processing technique. SFE is usually performed with pure or modified carbon dioxide, which facilitates off-line collection of extracts and on-line coupling with other analytical methods such as gas chromatography, high-performance liquid chromatography and supercritical fluid chromatography. In the search for environmental friendly solvents, increasing attention is being paid to supercritical carbon dioxide (SC-CO_2) for a wide variety of applications. Carbon dioxide is a nontoxic, inexpensive, nonflammable, and nonpolluting supercritical fluid solvent for the extraction of natural sources. Supercritical carbon dioxide extraction (SC-CO_2) is a simple, fast and effective technique as compared with conventional methods such as steam distillation and Soxhlet. This review presents key factors and challenges that should be addressed during the application of SFE technology. Furthermore, SFE has been compared with conventional extraction methods. This report provides a useful guide that can aid in the future development of efficient SFE process.

Keywords:

Bioactivecompounds; Carbon Dioxide; Conventional methods; Supercritical fluid extraction

Introduction

Solvents are used in large amounts in different industries such as food and pharmaceutical to separate different valuable bioactive compounds. Over the last decade, the design of green, efficient and sustainable extraction methods has received a great attention from researchers. Great improvements can be achieved with the use of non-conventional techniques such as supercritical carbon dioxide extraction(SC-CO_2), Ultrasound-Assisted Extraction (UAE) and Microwave-Assisted Extraction (MAE). In past decades, environmental friendly techniques are being interested to develop the "Green Chemistry" concept [1]. Therefore, an improved or better extraction technique is necessary. In the last 17 years (2000-2017), the extracts of more than 300 plant species have been studied using Supercritical Fluid Extraction (SFE) technology. The major share of SFE research covers plant material [2,3]. Many valuable pure components obtained from these plants are already in use for human nutrition and health purposes [4]. The most used solvent in supercritical state is carbon dioxide (CO_2) due to its great versatility, non-explosive, non-flammable, non-toxic and cost-efficient properties and easy to remove from the solutes [5]. CO_2 is classified as a low-critical temperature solvent. A good feature of low-critical temperature solvents, as compared with conventional liquid solvents, is that they operate at moderate temperature and provide thermo degradation of thermally labile compounds. These solvents are highly preferred in pharmaceutical and natural-product industries. A major advantage of low-critical temperature solvents is their easy separation from the extract [6]. Generally, supercritical carbon dioxide (SC-CO_2) which possesses properties of both liquids and gases has several major advantages compared with liquid solvents. Figure 1 shows the pressure-temperature phase diagram of CO_2. A pressure-temperature phase diagram of CO_2indicates the temperature and pressure conditions necessary for the various states of substance to exist. The critical temperature for carbon dioxide is 31.1°C, and the critical pressure is 73 atm. above the critical temperature and pressure, the fluid is called supercritical fluid. The isothermal compressibility of a fluid near its critical point is infinity, which translates into rapid change in its density as a function of temperature and pressure. The density of a supercritical fluid which affected the dissolving power is strongly tunable by varying the temperature or/and pressure. Therefore, selective fractions can be extracted from natural sources by carefully choosing the temperature and pressure operation[7,8].

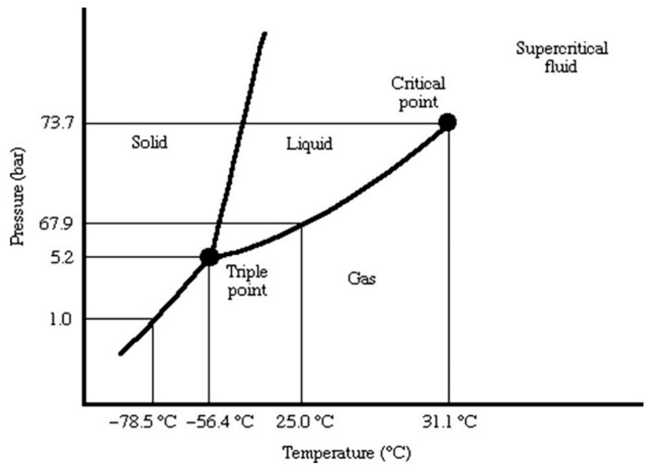

Figure 1: Pressure-Temperature phase diagram for CO_2.

A list of fluids which have been proposed as supercritical fluid solvent was shown in Table 1. It has been shown that N_2O cause violent explosions when used for samples having high organic content and should, therefore, be used only when absolutely necessary.The possible practical applications of super critical H_2O has been limited due to its high critical pressure and temperature ($T > 374$ ºC and $P > 221$ bar) together with thecorrosive nature of H_2O at these conditions [2].Other solvents (e.g. ethane, propane) have also been used in studies but their use is limited compared with CO_2 and for this reason the emphasis of this review is on SC-CO_2.

deMelo et al. (2014) presented a review regarding the plant species that have been studied under the scope of SFE. It has been stated that supercritical fluids have been mainly applied to the extraction valuable compounds from seeds and leaves which are followed by fruits, roots, flowers, rhizomes and bark [4]. Different valuable bioactive compounds including triglycerides, fatty acids, fatty alcohols, terpenoids, phytosterols, tocopherols, tocotrienols, and phenolics can be obtained applying SC-CO_2 from plant matrices.

A triglyceride is an ester derived from glycerol and three fatty acids. Triglycerides are the main constituents of body fat in humans and animals, as well as vegetable fat. Furthermore, it is known that their abundance in extracts lead to high quality biodiesel. Based on our knowledge there is lack of information about SFE application covering this purpose. Free fatty acids are also a specific family of compounds that occur independently in SFE extracts. In some cases the control of free fatty acid concentration may be helpful to quality control of the oils. Moreover, these compounds are key stones for soaps, oleochemical esters, oils and lubricants [9]. These compounds have been studied widely as target compounds for extraction, such as in SFE of borage (*Borage officinalis* L.) [10], primrose (*Oenotherabiennis* L.)[10],chinese star anise (*Illiciumverum*) [11], palm (*Elaesguineensis*)[12], pine (*Pinussylvestris* L.) [13], pupunha (*Guilielmaspeciosa*)[14], winter melon (*Benincasahispida*) seed[15, 16], spearmint (*Menthaspicata* L.) [17-19] and *Strobilanthescrispus*(pecahkaca)[20].

Fluid	Critical Temperature (T_c, K)	Critical Pressure (P_c, bar)	Critical Volume (V_c, $cm^3.mol^{-1}$)
Carbon dioxide	304.12	73.7	94.07
Ethane	305.3	48.7	145.5
Propane	369.8	42.5	200.0
Water	647.1	220.6	55.95
Ammonia	405.4	113.5	72.47
n-Hexane	507.5	30.2	368.0
Methanol	512.6	80.9	118.0

Table 1: Critical properties of fluids of interest in supercritical process.

Terpenoids are a large and diverse class of naturally occurring chemicals found in plant sources. These compounds are secondary metabolites whose role in plants is related to protection, pollination and growth mechanisms [21]. Plant terpenoids are used extensively for their aromatic qualities and play a role in traditional herbal remedies. The extraction of these compounds has been one of the major objectives driving SFE research. These compounds are classified to five subgroups according to the number of isoprene units. Monoterpenoids, with two isoprene units, such as geraniol [22,23]; sesquiterpenoids, three isoprene units, such as parthenolide [24]; diterpenoids, with four isoprene units, such as cafestol [25]; triterpernoids, with six isoprene units, such as ursolic acid [26-28]; tetraterpenoids, with eight isoprene units, such as lycopene[29, 30].

Phenolic compounds could act as hydrogen donators, singlet oxygen quenchers and reducing agents because of their redox properties [20]. Literatures pointed out phenolic compounds are responsible to reduce the risk of coronary heart diseases, stroke, cancer, degenerative and atherosclerosis diseases attributed to oxidative stress [18]. Phenolic compounds which present in edible and non-edible plants show various biological effects such as antioxidant activity. Plant materials crude extracts which contain high amount of phenolic compounds lead to reduce the rate of lipid oxidation and improve the quality of food products are strongly favoured in food industry. In addition, it was revealed that phenolic compounds like flavonoids can act as scavengers of Reactive Oxygen Species (ROS) through oxido-reductases inhibition [20]. Depending on the vegetable species, extracts obtained by SC-CO_2 can comprise substances from several phenolic groups like coumarins[31], cinnamic acids [32], quinones [33], flavonoids [17-20], lignans [32].

Selection of Operating Conditions

There are several parameters such as plant material preparation, selection of supercritical fluids, modifiers and extraction conditions which affected strongly the efficiency of SFE process. Hence, they should be considered carefully to develop a successful process.

Sample preparation

Preparation of plant materials is a critical step for SFE process. Fresh plant matrices contain high moisture content which cause mechanical problems due to ice formation. Furthermore, the efficiency of SFE process will reduce due to the high water-solubility of compounds dissolved in aqueous phase while the water solubility (0.3%) in SC-CO_2 is very low [34]. Therefore, it is necessary to control the moisture content of plant matrices by drying or mixing them with chemicals like sodium sulphate and silica gel. It has been stated that when the moisture content of *Benincasahispida* seeds was increased from 5 to 20% the crude extraction yield was decreased up to 38% [35]. Saldana et al., (2004) found that 10% moisture content was adequate to reach high recovery of β-carotene from apricot pomace by SC-CO_2 extraction. The plant matrices particle size could be considered as another critical parameter for SC-CO_2 extraction of nutraceuticals as the extraction process controlled by internal diffusion feed. The extraction time is extended by using larger particle size of samples. In contrast, fine powder can increase the rate of extraction; however, it is difficult to keep flow rate properly. By referring to different published literatures, it was believed that a smaller sample particle size results in greater extraction of lycopene by SC-CO_2[36-39].

Pressure and Temperature

The solvent properties of supercritical fluids may be tuned by changing pressure and temperature values, directly influencing density. The solubility of targeted compounds in SC-CO_2 is mainly determined by the SC-CO_2 density. In general, SC-CO_2 density increases with pressure at constant temperature and decreases with temperature at constant pressure, where the density decrease becomes smaller at higher pressures. The majority of the studies indicated that an increase in the extraction pressure of the supercritical carbon dioxide leads to an increase in the amount of valuable bioactive compounds extracted [6]. Bimakr et al. (2011) utilized pressure of 100 to 300 bar in the extraction of bioactive compounds spearmint (*Menthaspicata* L.) leaves. They found that the extraction yield increased with pressure from 100 to 200 bar, which was due to increase of SC-CO_2 density at higher pressures. However, an increase in the pressure level above 200 bar led to an unexpected reduction in the extraction yield. Liza et al. (2010) also found that at pressure above 200 bar there was non-existent of any flavonoid compounds. Moreover, same behavior was reported by Liu et al. (2009) in SCE of pomegranate (*Punicagranatum* L.) seeds. They found that an elevation of pressure (up to around 320 bar) caused significant increase of crude yield extract. They mentioned that this result most likely was due to the improvement of solute solubility resulted from the increased solvent density [39].

As mentioned above the density of CO_2 affected by the temperature. The density of CO_2 at constant pressure is reduced with increasing temperature and leading to reduce the solvent power of supercritical CO_2. Temperature also affects the volatility of the solute. Hence, the effect of a temperature elevation is difficult to predict because of its dependence on the nature of the sample. For a non-volatile solute, a higher temperature would result in lower extraction recovery owing to a decrease in solubility. A temperature increase may also cause breakdown of cell structure and increase the diffusion rate of the targeted compounds in the particles, therefore accelerating the extraction process [6]. Bimakr et al. (2011) studied the effect of temperature on SC-CO_2 extraction of bioactive compounds from spearmint leaves. They obtained that the extraction yield increased with temperature and the highest extraction yield (60.57 mg/g) was obtained at 60°C. In this manner, the solute vapour pressure played a key role leading to increase in the extraction yield [18].

Extraction Time

Extraction time is another important parameter that needs to be optimized for maximizing bioactive valuable compounds recovery from plant matrices. The extraction time could be helpful parameter to obtain a complete SC-CO_2 extraction. To enhance the efficiency of SC-CO_2 process it is necessary to prolong the contact time of the SC-$CO_2$with the sample material. Due to the physical structure of the seed, the penetration of the solvent and the diffusion of targeted compounds in the particles are very slow. Therefore, extraction time is usually limited to the fast extraction period since the amount of extraction yield recovered in the slow extraction period is negligible. Bimakr et al. (2013) examined the effect of extraction time at 60, 90 and 120 min on valuable compounds recovery from *Benincasahispida*seeds. They found that the highest crude extraction yield (176.30 mgextract/gdried sample) was obtained at 97 min. According to them, it was possible that 60 min of extraction time was insufficient for a complete extraction, while thermal degradation occurring at 120 min of extraction led to lowered yields of valuable bioactive compounds [16]. Reducing the extraction time could also reduce costs as well as improve energy efficiency [37]. In a study conducted by Ozkal et al. (2005) fast extraction period decreased from 183 to 64 and 32 min with a pressure increase from 30 to 45 and 60 MPa at 40°C. On the other hand, it decreased from 64 to 33 min with a temperature increase from 40°C to 50°C at 45 MPa. Furthermore, it was reported that, a 10-20 min static extraction prior to dynamic extraction improved the extract recoveries in SFE extraction of aflatoxins [40].

Bimakr et al. (2011) investigated the effect of dynamic time on the SC-CO_2 extraction of valuable compounds from *Menthaspicata* L. leaves. They concluded that the solvent power of SC-CO_2 is reduced at 100 bar pressure due to the lower CO_2 density so maximum yield was obtained during 90 min dynamic extraction time. Applying higher pressures (200 and 300 bar) the extraction rate is higher and as a consequence the extraction yield kept increasing up to 60 min dynamic extraction time[18]. In another study, Bimakr et al. (2016) shortened the extraction time using supercritical carbon dioxide extraction combined with pressure swing technique (SCE-PST). They found that application of pressurization-depressurization before continuous extraction time had a significant effect on improvement of extraction efficiency [15].

Fluid Flow Rate

The speed of the supercritical fluid flowing through the cell has a strong influence on the extraction efficiencies. The slower the fluid velocity, the deeper it penetrates the matrix. Papamichail et al. (2000) studied the SFE of oil from milled celery seeds using CO_2 as a solvent. They investigated the effect of flow rate of CO_2 on the extraction rate of celery seeds. They showed that the increase of the solvent flow rate leads to the increase of the amount of oil extracted versus extraction time [41]. Topal et al. (2006) tested SC-CO_2 flow rates ranging from 1.5 to 4.5 mL/min and found the highest lycopene yield at a flow rate of 2.5 mL/min. Using the flow rate between 2.5 to 4.5 mL/min a decrease in the amount lycopene extracted was observed [38].

Co-solvent Flow Rate

An important shortcoming of the use of SC-CO_2 is its low polarity. Considering the chemical nature of most natural bioactive compounds, generally polar compounds, CO_2 alone may not be able to extract them. To cope with this issue, co-solvents (also called modifiers) are employed during extraction at small proportions (typically, 1-10%). These co-solvents are solvents with higher polarity than CO_2, expanding the range of compounds attainable by increasing the polarity of the supercritical mixture[18]. According to Shi et al. (2009), due to the non-toxic properties of water and ethanol, these two compounds may be used in place of other organic solvents for the extraction of bioactive compounds [42]. In different studies it has been concluded that adding ethanol (5-30%) is needed to enhance the phenolic compounds solubility in SC-CO_2 of grape seeds [43], olive leaves [44], grape skin [45], pistachio hulls [46], apple, peach [47] and sour cherry pomaces[48]. Bimakr et al. (2011) investigated the effect of co-solvent flow rate (3-9 g/min) on antioxidant activities of SC-CO_2 extracts of spearmint leaves. They found that the highest antioxidant activity of SC-CO_2 extracts was obtained by using 9 g/min (63.13%). The obtained SC-CO_2 extracts antioxidant activity using 9 comparing to 6 g/min was higher but the difference between them is too low (1.46%) and it is not significant. Therefore, 6 g/min co-solvent flow rate is preferable due to its better effect on the antioxidant activity of obtained SC-CO_2 extracts and economic cost. They conclude considering the polarity of bioactive compounds such as phenolic compounds which contributed greatly on the antioxidant activity of spearmint leaves extracts by increasing co-solvent flow rate (ethanol) the antioxidant activity was increased[18].

Instrumentation

Depending on the process developed the instrumentation needed can be more or less complex. Figure 2 showed a schematic diagram of the SFE system. It is composed of solvent and modifier pumps, extractor vessel with temperature control, pressure restrictor and collection vessel. Circulated deionized water at 5°C was used for cooling different zones in the SC-CO_2 extraction system. The instrument may be also made more complicated by adding fractionation vessels equipped with independent pressure and temperature controls. To collect volatile compounds the system could be equipped with CO_2 recycling system or refrigerated trap. It is evident that the complexity of the SC-CO_2system will depend on the scale. Several recent reviews dealt with the recovery of bioactive compounds from plants using SFE from a more or less broad perspective [49,50]. Huang et al. (2017) presented a good review aboutthe-oretical models for supercritical fluid extraction which could be helpful for researchers [51].

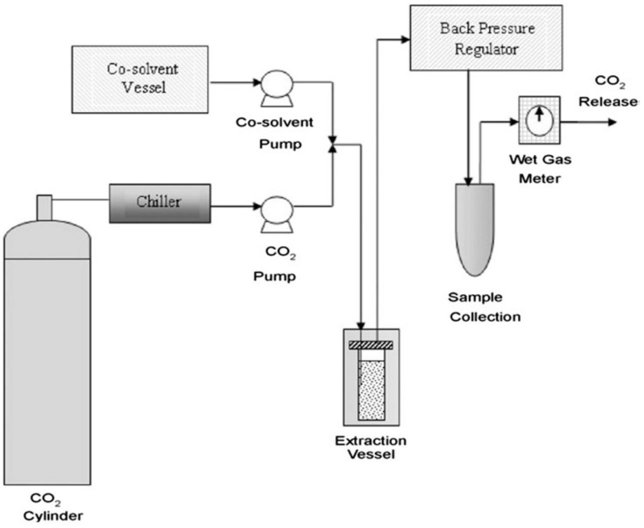

Figure2: A schematic design of the supercritical fluid extractor unit [20].

It must be kept in mind that the industrialization of SCE system is very limited due to the fact that CO_2 possesses non-polar properties. In order to extract polar compounds it is necessary to add some polar solvents as modifier since they are soluble in carbon dioxide. As this new emerging technology is very expensive due to its high investment costs so it should compete with the worldwide opinion regarding the cost issues. Different studies focused on development of a scaling-up strategies and they concluded that for a process to reach an adequate scale-up level, it is expected that it has been previously assessed upon optimization of operating conditions, selection of preferable extraction times, and modeling of the process [4,12,17,25,30].

Comparison of supercritical fluid extraction to conventional methods

There are different classical methods to extract valuable compounds from plant matrices such as hydrostillation, Soxhlet and maceration. The principle of these methods is solvent choice coupled with heat and/or agitation. One of the most common extraction procedures which have been used over 100 years is conventional Soxhlet extraction. This method has developed by von Soxhlet in 1879 and is considered as the main reference to evaluate the other solid-liquid extraction methods performance [34]. The time for an average Soxhlet extraction ranges from 1 to 72 h. The completed extraction produces a high volume, dilute solution which usually needs to be concentrated prior to analysis. The main limiting step of this method is the extraction of thermo liable compounds which are degraded at high temperature during long extraction time [18].

The advantages of SC-CO_2process over other conventional processes such as extraction by solvents and separation by distillation are automation, the reduction in operational steps, safe operation due to the use of nonorganic solvents and the use of moderate temperature in the critical range favorable for heat labile foods. The main advantage of SC-CO_2 extraction techniqueis the excellent quality of the resulting product [52].

Several researchers have compared supercritical fluid extraction with conventional extraction methods. A extraction yield obtained with SC-CO_2 method was similar to those from a hot hexane extraction [53]. Myer et al. (1992) reported that SC-CO_2 method obtained recoveries from 97% to 100% of a Soxhlet extraction in potato chips and puff-dried products [54]. King et al. (1996) concluded that there were no significant differences between fatty acids extracted from beef samples with an SFE method and with the solvent extraction [55].

Seed and nut oils are traditionally separated mechanical pressing of organic solvents. Undesirable solvent residue in the final product cannot be avoided using organic solvent extraction. SC-CO_2 extraction is also used to extract seed and nut oils. It has been demonstrated that walnut oil extracted by SC-CO_2 had a higher amount of tocopherols (405.7 μg/g oil) compared with the oil obtained with hexane (303.2 μg/ g oil [56]. In different studies it is stated that the oil extracted by SC-CO_2 was clearer than that obtained by organic solvent extraction, indicating the need for less refining process [6,16].

Donelian et al. (2009) compared extraction of patchouli (*Pogostemoncablin*) essential oil with SC-CO_2 and by steam distillation. They found that the extraction of patchouli essential oil with SC-CO_2 at 14MPa and 40°C gave the best yield (5.07%), which was higher than that of steam distillation (of 1.50%) [57]. Application of supercritical carbon dioxide extraction was investigated by Bimakr et al. (2013) to separate valuable compounds from *Benincasahispida* seeds. Optimal process condition were identified by using response surface methodology and the results demonstrated that the combined treatment of 234.25 bar of pressure, 46°C of temperature and 95.05 min of dynamic extraction time was required for maximizing crude extraction yield (174.91 mg/g) and antioxidant activity (52.96% inhibition of DPPH free radicals), and total phenolic content (40.45 mg GAE/g extract) of extracts. They concluded that the quantity and quality of extracts obtained under optimum condition of SC-CO_2extraction was better than those obtained at optimized ultrasound-assisted extraction [16].

The efficiency of different environment friendly techniques including ultrasound-assisted extraction [58], supercritical carbon dioxide extraction [16], and supercritical carbon dioxide extraction combined with pressure swing technique [15] were compared for separation of valuable compounds from winter melon (*Benincasahispida*) seeds. They reported that application of various extraction techniques resulted in extracts that differ in quality and quantity of crude extract. They concluded that remarkable variations in crude extraction yield, rradical scavenging activity, and total phenolic content of *Benincasahispida* seeds extract were found depending on the extraction technique. Higher crude extraction yield could be obtained by Soxhlet extraction with lower separation of bioactive compounds as they are thermo sensitive compounds and may be degraded during Soxhlet extraction. In contrast, using ultrasound-assisted extraction, SC-CO_2 extraction, and SC-CO_2 extraction lead to lower quantity of crude extraction yield with better quality in terms of valuable bioactive compounds separation.

Piggott et al. (1997) investigated different extraction methods including steam distillation, solvent extraction, supercritical fluid extraction and liquid CO_2 extraction to obtain the volatile oil from Western Australian sandalwood. They revealed that the highest yields of extractable material and total volatile compounds was obtained applying SC-CO_2 [59].

Extraction of essential oils from *Grapefruit flavedo* were studied applying hydrodistillation and solvent extraction using different solvents such as pentane, ethanol and supercritical carbon dioxide [60]. Monoterpene hydrocarbons decrease in supercritical carbon dioxide extracts at 87-90% with respect to their quantity in pentane extracts (95%) and in hydrodistillate (97%) these levels in monoterpene hydrocarbons were related to the limonene content, the most abundant compound in grapefruit essence. Sesquiterpenes, aldehydes, alcohols and esters increased in supercritical carbon dioxide extracts obtained at a high fluid density.

Silva et al. (2016) provided a good review paper regarding different studies which applied SCE technique for extraction

Phytochemicals	Plants	Solvent	Extraction methoda	Extraction time (min)	Yield	Reference
Tocols	Amaranthuscau-datus	Methanol	SOX (25ºC)	1440	76.32 mg/kg	[62]
		Methanol	UAE (25ºC)	60	63.7 mg/kg	
		CO_2	SFE (25ºC, 400 atm)	15	129.27 mg/kg	
β -Sitosterol/	Okra seed	n-Hexane	SOX	-	2010 mg/kg	[63]
					127 mg/kg	
α-Tocopherol/		Ethanol	SOX	-	380 mg/kg	
γ-Tocopherol		CO_2	SFE(50ºC, 450 bar)	240-800		
Saponins	Ginseng	Methanol (80%)	CSE (75ºC)	180	5.24 g/100g	[64]
		Methanol (80%)				
			MAE (75ºC)	0.5	5.31 g/100g	
Naringin	Citrus paradisi	Ethanol (70%)	SOX	480	15.2 g/kg	[65]
		CO2 - ethanol	SFE (58.6ºC, 95 bar)	45	14.4 g/kg	
Carvone/limone	Caraway seeds	n-Hexane	SOX	300	16.28 mg/g	[66]
		n-Hexane	UAE (69ºC)	60	14.45 mg/g	
		n-Hexane	UAE (20-38ºC)	60	17.16 mg/g	
Oil	Rose hip seeds	n-Hexane	SOX	180	48.5 g/kg	[67]
		n-Hexane				
			UAE (69ºC)	60	32.5 g/kg	
		n-Hexane				
			MAE (40ºC))	30	52.6 g/kg	
		CO2	SFE (35ºC, 250bar)			
			SFE (28ºC, 100bar)	80	57.2 g/kg	
		CO2- propane				
				35	66.8 g/kg	
Catechin	Spearmint leaves	Ethanol	SOX	240	0.081 mg/g	[19]
				60	0.141 mg/g	
		CO2- ethanol	SFE (60ºC, 200bar)			
Epicatechin	Spearmint leaves	Ethanol	SOX	240	0.114 mg/g	[18]
			SFE (60ºC, 200bar)	60	0.156 mg/g	
		CO2- ethanol				
Rutin	Spearmint leaves	Methanol	SOX	240	0.161 mg/g	[17]
			SFE (60ºC, 200bar)	60	0.148 mg/g	
		CO2- ethanol				
Myricetin	Spearmint leaves	Petroleum ether CO2- ethanol	SOX	240	-	[18]
			SFE (60ºC, 200bar)	60	0.117 mg/g	
Luteolin	Spearmint leaves	Ethanol (70%)	SOX	240	0.146 mg/g	[19]
			SFE (60ºC, 200bar)	60	0.657 mg/g	
		CO2- ethanol				
Apigenin	Spearmint leaves	Ethanol	SOX	240	0.246 mg/g	[18]
			SFE (60ºC, 200bar)	60	0.270 mg/g	
		CO2- ethanol				
Naringenin	Spearmint leaves	Ethanol (70%)	SOX	240	-	[19]
			SFE (60ºC, 200bar)	60	0.249 mg/g	
		CO2- ethanol				

Gallic acid	Winter melon seeds	Ethanol	SOX	360	-	[68, 69]
				60		
		CO2- ethanol	SFE (100 bar, 40°C)	120	0.210 mg/g	
				180		
			SFE (300 bar, 50°C)		0.610 mg/g	
			SFE (450 bar, 60°C)		0.540 mg/g	
Catechin	Winter melon seeds	Ethanol	SOX	360	-	[68, 69]
				60		
		CO2- ethanol	SFE (100 bar, 40°C)	120	-	
				180		
			SFE (300 bar, 50°C)		0.250 mg/g	
			SFE (450 bar, 60°C)		0.220 mg/g	
Naringenin	Winter melon seeds	Ethanol	SOX	360	0.120 mg/g	[68, 69]
				60		
		CO2- ethanol	SFE (100 bar, 40°C)	120	0.260 mg/g	
				180		
			SFE (300 bar, 50°C)		0.270 mg/g	
			SFE (450 bar, 60°C)			
Myrecitin	Winter melon seeds	Ethanol	SOX	360	-	[68, 69]
				60	0.140 mg/g	
		CO2- ethanol	SFE (100 bar, 40°C)	120		
				180	0.110 mg/g	
			SFE (300 bar, 50°C)			
			SFE (450 bar, 60°C)			
Quercetin	Winter melon seeds	Ethanol	SOX	360	0.110 mg/g	[68, 69]
				60		
		CO2- ethanol	SFE (100 bar, 40°C)	120	0.230 mg/g	
			SFE (300 bar, 50°C)	180	0.160 mg/g	
			SFE (450 bar, 60°C)			
Oil	Winter melon seeds	Ethanol	SOX	360	250 mg/g	[68-71]
		Ethanol	UAE (52°C, 65% amplitude)	36	108.62 mg/g	
		CO2- ethanol	SFE (244 bar, 46°C)	97	175.60 mg/g	
		CO2- ethanol	SFE-PST (181 bar, 46°C)	50	235.70 mg/g	
Ergothioneine	Pleurotusostreatus	CO2- ethanol	SFE (210 bar, 48°C)	80	1.35 mg/g	[72]
Camphor	Rosemary leaves	CO2	SFE (300 bar, 40°C)	60	0.132 g/g	[73]
		CO2- ethanol	SFE (150 bar, 40°C)	60	0.227 g/g	

[a]SOX, Soxhlet extraction; UAE, Ultrasound-Assisted Extraction; MAE, Microwave-Assisted Extraction; SFE, Supercritical Fluid Extraction; and SFE-PST, Supercritical Fluid Extraction combined with Pressure Swing Technique

Table 2: Comparison of different extraction methods for selected bioactive compounds.

of different valuable bioactive compounds from natural sources. It can be very helpful for researchers in this field of study [61]. Furthermore, supercritical fluid extraction of different valuable compounds from various sources in different studies is presented in Table 2.

Conclusion

The use of supercritical fluids, especially carbon dioxide, in the extraction of bioactive components from natural sources has increased in recent years due to the key advantages of the supercritical extraction process. Carbon dioxide is widely applied in its supercritical state for extraction of bioactive compounds which could be due to its “health and safety” and environmental nature and relate to increased unease about the presence of organic solvent residues in material for human consumption.The supercritical fluid extraction operation is based on the solvating properties of supercritical fluid, the characteristics of which are achieved by employing pressure and temperature that surpasses the critical point of the fluid. Many studies have shown that SC-CO_2 is effective in extraction of valuable compounds. It has been stated that the extraction efficiency in terms of yield and composition are affected by different factors such as sample preparation (particle size and moisture content) and extraction parameters (pressure, temperature, solvent flow rate, extraction time, and use of a cosolvent). Moreover, SC-CO_2 extraction system can be used with supercritical fluid fractionation and supercritical fluid chromatography to purify and identify the extracted compounds. SC-CO_2extraction can be a true alternative for obtaining high quality extracts from several natural sources.

References

1. Kamran Khan M, Abert-Vian M, Fabiano-Tixier AS, Dangles O, Chemat F (2010) Ultrasound-Assisted Extraction of Polyphenols (Flavanone Glycosides) from Orange (Citrus sinensis L.) Peel. Food Chem 119: 851-858.
2. Brunner G (2010) Applications of Supercritical Fluids. Annu Rev Chem Biomol Eng 1: 321-342.
3. Souza Machado BA, Pereira CG, Nunes SB, Padilha FF, Umsza-Guez MA (2013) Supercritical Fluid Extraction Using CO_2: Main Applications and Future Perspectives. Sep SciTechnol 48: 2741-2760.
4. deMelo MMR, Silvestre AJD, Silva CM (2014) Supercritical Fluid Extraction of Vegetable Matrices: Applications, Trends and Future Perspectives of a Convincing Green Technology. J Supercrit Fluids 92: 115-176.
5. Chiu KL, Cheng YC, Chen JH, Chang CJ, Yang PW (2002) Supercritical Fluids Extraction of Ginkgo ginkgolides and Flavonoids. J Supercrit Fluids 24: 77-87.
6. Martinez JL (2008) Supercritical Fluid Extraction of Nutraceuticals and Bioactive Compounds. New York: United States of America, CRC Press.
7. Luque de Castro MD, Priego-Capote F (2010) Soxhlet Extraction: Past and Present Panacea. J Chromatogr A 1217: 2383-2389.
8. Yen HW, Yang SC, Chen CH, Jesisca A, Chang JS (2015) Supercritical Fluid Extraction of Valuable Compounds from Microalgal Biomass. BioresourceTechnol 184: 291-296.
9. Hill K, Hofer R (2009) Natural Fats and Oils.In: Hofer R (Ed.), Sustainable Solutions for Modern Economies, RSC, Cambridge.
10. Kotnik P, Skerget M, Knez Z (2006) Kinetics of Supercritical Carbon Dioxide Extraction of Boragea Evening Primrose Seed Oil. Eur J Lipid SciTechnol 108: 569-576.
11. Li GL, Sun ZW, Xia LA, Shi JY, Liu YJ, et al. (2010) Supercritical CO_2 Oil Extraction from Chinese Star Anise Seed and Simultaneous Compositional Analysis using HPLC by Fluorescence Detection and Online Atmospheric CI-MS Identification. J Sci Food Agr 90: 1905-1913.
12. de Franca LF, Meireles MAA (2000) Modeling the Extraction of Carotene and Lipids from Pressed Palm Oil (Elaesguineensis) Fibers using Supercritical CO_2. J Supercrit Fluids 18: 35-47.
13. Arshadi M, Hunt AJ, Clark JH (2012) Supercritical Fluid Extraction (SFE) as an Effective Tool in Reducing Auto-Oxidation of Dried Pine Sawdust for Power Generation. RSC Advances 2: 1806-1809.
14. Araujo ME, Machado NT, Franca LF, Meireles MAA (2000) Supercritical extraction of pupunha (Guilielmaspeciosa) Oil in a Fixed Bed using Carbon Dioxide. Braz J ChemEng 17: 1678-4383.
15. Bimakr M, Russly AR, Farah ST, Noranizan MA, Zaidul ISM, et al. (2016) Characterization of Valuable Compounds from Winter Melon (Benincasahispida (Thunb.) Cogn.) Seeds Using Supercritical Carbon Dioxide Extraction Combined with Pressure Swing Technique.Food Bioprocess Technol 9: 396-406.
16. Bimakr M, Russly AR, Farah ST, Noranizan MA, Zaidul ISM, et al. (2013) Supercritical Carbon Dioxide Extraction of Seed Oil from Winter Melon (BenincasaHispida) and Its Antioxidant Activity and Fatty Acid Composition. Molecules 18: 997-1014.
17. Mandana B, Russly AR, Ali G, Farah ST, Liza MDS, et al. (2012) Optimization of Supercritical Carbon Dioxide Extraction of Bioactive Flavonoid Compounds from Spearmint (Menthaspicata L.) Leaves by Using Response Surface Methodology.Food Bioprocess Technol 5: 912-921.
18. Mandana B, Russly AR, Ali G, Farah ST, Liza MDS, et al. (2011) Comparison of Different Extraction Techniques for Isolation of Major Bioactive Flavonoid Compounds from Spearmint (MenthaSpicata L.) Leaves. Food Bioprod Process 89: 67-72.
19. Mandana B, Russly AR, Ali G, Farah ST (2011) Antioxidant Activity of Spearmint (MenthaSpicata L.) Leaves Extractsby Supercritical Carbon Dioxide (SC-CO_2) Extraction. Int Food Res J 18: 543-547.
20. Liza MS, Abdul Rahman R, Mandana B, Jinap S, Rahmat A, et al. (2012) Supercritical Fluid Extraction Of Bioactive Flavonoid from Strobilanthescrispus(pecahkaca) and Its Comparison With Solvent Extraction. Int Food Res J 19: 503-508.
21. Arroo R and Eberhard B (2007) Terpenes-flavors, fragrances, pharmaca, pheromones. Wiley-VCH, 2006, 214 pp ISBN 3-527-31786-4, Applied Organometallic Chemistry 21: 377-385.
22. Kakasy AZ, Lemberkovics E, Simandi B, Lelik L, Hethelyi E, et al. (2006) Comparative Study of Traditional Essential Oil and Supercritical Fluidextracts of Moldavian Dragonhead (Dracocephalummoldavica L.). Flavour Frag J 21: 598-603.
23. Peterson A, Machmudah S, Roy BC, Goto M, Sasaki M, et al. (2006) Extraction of Essential Oil From Geranium (Pelargonium graveolens) with Supercritical Carbon Dioxide. J Chem Technol Biot 81: 167-172.
24. Cretnik L, Skerget M, Knez Z (2005) Separation of Parthenolide from Feverfew: Performance of Conventional and High-Pressure Extraction Techniques. Sep PurifTechnol 41:13-20.
25. Barbosa HMA, de Melo MMR, Coimbra MA, Passos CP, Silva CM (2014) Optimization of the Supercritical Fluid Coextraction of Oil and Diterpenes from spent Coffee Grounds Using Experimental Design and Response Surface Methodology. J Supercrit Fluids 85: 165-172.
26. Domingues RMA, de Melo MMR, Neto CP, Silvestre AJD, Silva CM (2012) Measurement and Modeling of Supercritical Fluid Extraction Curves of Eucalyptus Globulus Bark: Influence of the Operating Conditions upon Yields and Extract Composition. J Supercrit Fluids 72: 176-185.
27. Domingues RMA, de Melo MMR. Oliveira ELG, Neto CP, Silvestre AJD, et al. (2013) Optimization of the Supercritical Fluid Extraction Of Triterpenicacids from Eucalyptus Globulus Bark Using Experimental Design. J Supercrit Fluids 74: 105-114.
28. Domingues RMA, Oliveira ELG, Freire CSR, Couto RM, Simoes PC, et al. (2012) Supercritical Fluid Extraction of Eucalyptus Globulus Bark-a Promising Approach for Triterpenoid Production. Int J Mol Sci 13: 7648-7662.
29. Katherine LSV, Edgar CC, Jerry WK, Luke RH, Julie CD (2008) Extraction Conditions Affecting Supercritical Fluid Extraction (SFE) of Lycopene from Watermelon. BioresourceTechnol 99: 7835-7841.
30. Machmudah S, Martin A, Sasaki M, Goto M (2012) Mathematical Modeling for Simultaneous Extraction and Fractionation Process of Coffee Beans with Supercritical CO_2 and Water. J Supercrit Fluids 66: 111-119.
31. Pokrovskii OI, Markoliya AA, Lepeshkin FD, Kuvykin IV, Parenago OO, et al. (2009) Extraction of Linear Furocoumarins from AmmiMajus Seeds by Means of Supercritical Fluid Extraction and Supercritical Fluid Chromatography. Russ J Phys Chem B 3: 1165-1171.
32. Sovova H, Opletal L, Bartlova M, Sajfrtova M, Krenkova M (2007) Supercritical Fluid Extraction of lignans and Cinnamic Acid from SchisandraChinensis. J Supercrit Fluids 42: 88-95.
33. Solati Z, Baharin S, Bagheri H (2012) Supercritical Carbon Dioxide (SC-CO_2) Extraction of Nigella Sativa L. Oil Using Full Factorial Design. Ind Crop Prod 36: 519-523.
34. Wang L, Weller C L (2006) Recent Advances in Extraction of Nutraceuticals from Plants. Trends Food SciTechnol 17: 300-312.
35. Saldana MDA, Temelli F, Guigard SE, Tomberli B, Gray CG (2010) ApparentSolubility of Lycopene and β-carotene in Supercritical CO_2, CO_2 + ethanol andCO_2 + Canola Oil Using Dynamic Extraction of Tomatoes. J Food Eng 99: 1-8.
36. Nobre BP, Palavra AF, Pessoa FLP, Mendes RL (2009) Supercritical CO_2 Extraction of Trans-Lycopene from Portuguese Tomato Industrial Waste. FoodChem 116: 680-685.

37. Baysal T, Ersus S, Starmans DAJ (2000) Supercritical CO$_2$ Extraction of β-caroteneand Lycopene from Tomato Paste Waste. J Agr Food Chem 48: 5507-5511.
38. Topal U, Sasaki M, Goto M, Hayakawa K (2006) Extraction of Lycopene fromTomato Skin with Supercritical Carbon Dioxide: Effect of Operating Conditionsand Solubility Analysis. J Agr Food Chem 54: 5604-5610.
39. Liu G, Xu X, Hao Q, Gao Y (2009) Supercritical CO$_2$ Extraction Optimization of Pomegranate (Punicagranatum L.) Seed Oil Using Response Surface Methodology. LWT - Food SciTechnol 42: 1491-1495.
40. Ozkal SG, Salgin U, Yener ME (2005) Supercritical Carbon Dioxide Extraction of hazelnut Oil. J Food Eng 69: 217-224.
41. Papamichail I, Louli V, Magoulas KJ (2000) Supercritical Fluid Extraction of Celery Seed Oil.J Supercrit Fluids 18: 213-226.
42. Shi J, Yi C, Xue SJ, Jiang Y, Ma Y, et al. (2009) Effects of Modifiers on the Profile of Lycopene Extracted from Tomato Skins by Supercritical CO$_2$. J Food Eng 93: 431-436.
43. Murga R, Ruiz R, Bettran S, Cabezas JL (2000) Extraction of Natural Complex Phenols and Tanins from Grapes Seeds by Using Supercritical Mixtures Of Carbon Dioxide and Alcohol. J Agr Food Chem 48: 3408-3412.
44. Le Floch F, Tena MT, Rios A, Valcarcel M (1998) Supercritical Fluid Extraction of Phenol Compounds from Olive Leaves. Talanta 46: 1123-1130.
45. Chafer A, Fornari T, Berna A, Stateva RP (2004) Solubility of Quercetin in Supercritical CO$_2$ + Ethanol as a Modifier: Measurements and Thermodynamic Modeling. J Supercrit Fluids 32: 89-96.
46. Goli A, Barzegar M, Sahari M (2005) Antioxidant Activity and Total Phenolic Compounds of Pistachio (Pistachia Vera) Hull Extracts. Food Chem 92: 521-525.
47. Adil HI, Cetin ME, Yener A (2007) Subcritical (Carbon Dioxide + Ethanol) Extraction of Polyphenols from Apple and Peach Pomaces, and Determination of the Antioxidant Activities of the Extracts. J Supercrit Fluids 43: 55-63.
48. Adil IH, Yener ME, Bayindirli A (2008) Extraction of Total Phenolics from Sour Cherry Pomace by High Pressure Solvent and Subcritical Fluid and Determination of the Antioxidant Activities of the Extracts. Sep SciTechnol 43: 1091-1110.
49. Gonzalez-Coloma A, Martin L, Mainar AM, Urieta JS, Fraga BM, et al. (2012) Supercritical Extraction and Supercritical Antisolvent Fractionation of Natural Products from Plant Material: Comparative Results on Perseaindica. Phytochem Rev 11: 433-446.
50. Herrero M, Sanchez-Camargo A, Cifuentes A, Ibanez E (2015)Plants, Seaweeds, Microalgae and Food By-Products as Natural Sources of Functional Ingredients Obtained Using Pressurized Liquid Extraction and Supercritical Fluid Extraction. Trends Anal Chem 71: 26-38.
51. Zhen H, Xiao S, Jiang W (2012) Theoretical Models for Supercritical Fluid Extraction. JChromatogr A 1250: 2-26.
52. Sahena F, Zaidul ISM, Jinap S, Karim AA, Abbas KA, et al. (2009) Application of Supercritical CO$_2$in Lipid Extraction. J Food Eng 95: 240-253.
53. Ikushima Y, Saito N, Hatakeda K, Ito S, Asano T, et al. (1986) A Supercritical Carbon Dioxide Extraction from Mackarel (scomberjaponicus) Powder: Experiment and Modelling. Bulletin of the Chemical Society of Japan 59: 3709-3713.
54. Myer L, Damian J, Liescheski P, Tehrani J (1992) Supercritical. Fluid Extraction of Plant Materials. Isco: Lincoln, NE.
55. King JW, Eller FJ, Snyder JM, Johnson JH, Mc Keith FK, et al. (1996) Extraction of Fat from Ground Beef for Nutrient Analysis Using Analytical Supercritical Fluid Extraction. J Agr Food Chem 44: 2700-2704.
56. Nagesha GK, Manohar B, UdavaSankar K (2017) Enrichment of Tocopherols in Modified Soy Deodorizer Distillate Using Supercritical Carbon Dioxide Extraction. Eur Food Res Technol 217: 427-433.
57. Doneliana LHC, Carlson TJ, Lopes RAF, Machado A (2009) Comparison of Extraction of Patchouli (Pogostemoncablin) Essential Oil with Supercritical CO$_2$ and by Steam Distillation. J Supercrit Fluids 48: 15-20.
58. Mandana B, Russly AR, Farah ST, Noranizan MA, Zaidul ISM, et al. (2012) Optimization of Ultrasound-Assisted Extraction of Crude Oil from Winter Melon (Benincasahispida) Seed Using Response Surface Methodology and Evaluation of Its Antioxidant Activity, Total Phenolic Content and Fatty Acid Composition. Molecules 17: 11748-11762.
59. Piggott MJ, Ghisalbeti EL, Trengove RD (1997) Western Australian Sandalwood Oil: Extraction by Different Techniques and Variations of the Major Components in Different Sections of a Single Tree. FlavourFragr J 12: 43-46.
60. Poiana M, Sicari V, Mincione B (1998) Supercritical Carbon Dioxide (SC□ CO$_2$) Extraction of Grapefruit Flavedo.FlavourFragr J 13: 125-130.
61. da Silva RPFF, Rocha-Santos TAP, Duarte AC (2016) Supercritical Fluid Extraction of Bioactive Compounds. Trends Anal Chem 76: 40-51.
62. Bruni R, Guerrini A, Scalia S, Romagnoli C, Sacchetti G (2002) Rapid Techniques for the Extraction of Vitamin E Isomers from Amaranthuscaudatus-Seeds: Ultrasonic and Supercritical Fluid Extraction.Phytochem Anal 13: 257-261.
63. Andras CD, Simandi B, Orsi F, Lambrou C, Missopolinou- Tatala D, et al. (2005) Supercritical Carbon Dioxide Extraction of Okra (Hibiscus esculentusL.) Seeds.J Sci Food Agric 85: 1415-1419.
64. Kwon JH, Belanger JM, Pare JR (2003) Optimization of Microwave-Assisted Extraction (MAP) for Ginseng Components by Response Surface Methodology. J Agric Food Chem 51: 1807-1810.
65. Giannuzzo AN, Boggetti HJ, Nazareno MA, Mishima HT (2003) Supercritical Fluid Extraction of Naringin from the Peel of Citrus Paradise.Phytochem Anal 14: 221-223.
66. Chemat S, Lagha A, AitAmar H, Bartels PV, Chemat F (2004) Comparison of Conventional and Ultrasound-Assisted Extraction of Carvone and Limonene from Caraway Seeds. Flavour Frag J 19: 188-195.
67. Szentmihalyi K, Vinkler P, Lakaos B, Then M (2002) Rose Hip (Rosa canina L.) Oil Obtained from Waste Hip Seeds by Different Extraction Methods. BioresourTechnol 82: 195-201.
68. Bimakr M, Russly AR, Farah ST, Noranizan MA, Zaidul ISM, et al.(2013) Ultrasound-Assisted Extraction of Valuable Compounds from Winter Melon(Benincasahispida) Seeds. Inter Food Res J 20: 331-338.
69. Bimakr M, Russly AR,Ganjloo A (2015) Winter Melon (Benincasa hispida) Seeds and Impact Of Extraction On Compositionto the book Food Processing and Impact on Active components. Academic Press (Elsevier). ISBN: 978-0-12-404699-3.
70. Bimakr M, Russly AR, Farah ST, Noranizan MA, Zaidul ISM, et al.(2012) Optimization ofUltrasound-Assisted Extraction of Crude Oil fromWinter Melon (Benincasahispida) Seed using Response Surface Methodologyand Evaluation of its Antioxidant Activity, Total Phenolic Content andFatty Acid Composition. Molecules 17: 11748-11762.
71. Bimakr M, Russly AR, Farah ST, Noranizan MA, Zaidul ISM, et al. (2013) Ultrasound-Assisted Extraction of Valuable Compounds from Winter Melon(Benincasahispida)Seeds. International Food Research Journal 20: 331-338.
72. Bhattacharya M, Srivastav PP, Mishra HN (2014) Optimization of Process Variablesfor Supercritical Fluid Extraction of Ergothioneine and Polyphenols from Pleurotusostreatus and Correlation to Free-Radical Scavenging Activity. J Supercrit Fluids 95: 51-59.
73. Fornari T, Vincente G, Vazquez E, Garcia-Risco MR, Reglero G, et al. (2012) Isolation of Essential Oil from Different Plants and Herbs by Supercritical Fluid Extraction. J Chromatogr A 1250: 34-48.