3 Supercritical Fluid Extraction in Food Analysis

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3.1 INTRODUCTION

This chapter is an overview of the current state of the science and technology of supercritical fluids. The principal objective is to acquaint the reader with the unusual properties of supercritical fluids, and
with the ways some basic principles are essential in understanding the supercritical fluid extraction (SFE) technique and the independence of relevant process parameters that are exploited for a variety of applications in cases of both SFE and supercritical fluid chromatography (SFC) in the food industry. The unusual solvent properties of supercritical fluids, together with their thermodynamic behavior near a critical point, are explained within the framework of fluid-phase diagrams. Characterizing the behavior of supercritical fluids still offers many challenges to scientists. Engineers have exploited the peculiarities of supercritical fluids to great advantage to design new instruments and processes. These proceedings are an example of the dialogue between scientists and engineers that is needed to deepen the understanding of this interesting medium and to widen the field of applications.

The basic philosophy of utilization is centered on the fact that the properties of supercritical fluids can be varied from gas-like to liquid-like values by simply adjusting the pressure. These fluids are therefore very attractive as tunable process solvents or reaction media.

To summarize, in this chapter the basic knowledge and terminology required for understanding supercritical fluid applications including SFE together with SFC are introduced at an elementary level.

### 3.2 Basic Definitions

#### 3.2.1 Critical Temperature

The critical temperature ($T_c$) is the maximum temperature at the critical point at which a gas can be converted into a liquid by an increase in pressure.

#### 3.2.2 Critical Pressure

The critical pressure ($P_c$) is the minimum pressure that would suffice to liquefy a substance at its critical temperature. Above the critical pressure, increasing the temperature will not cause a fluid to vaporize to give a two-phase system.

#### 3.2.3 Critical Point

The characteristic temperature ($T_c$) and pressure ($P_c$) above which a gas cannot be liquefied.

#### 3.2.4 Supercritical Fluid

The defined state of a compound, mixture, or element above its critical pressure ($P_c$) and critical temperature ($T_c$). It is a gas-like, compressible fluid that takes a shape of its container and fills it. It is not a liquid but has liquid-like densities (0.1–1 g/mL) and solvating power.

#### 3.2.5 Reduced Temperature

The reduced temperature ($T_r$) is the ratio of the temperature ($T$) in the system to the critical temperature ($T_c$).

$$ T_r = \frac{T}{T_c} \quad (3.1) $$

#### 3.2.6 Reduced Pressure

The reduced pressure ($P_r$) is the ratio of the pressure in the system ($P$) to the critical pressure ($P_c$).

$$ P_r = \frac{P}{P_c} \quad (3.2) $$
3.2.7 SuperCritical Fluid Extraction

Extraction of a material using a supercritical fluid. The extracted material is usually recovered by reducing the pressure or increasing the temperature of the extraction fluid and allowing the volatile components of the mobile phase to evaporate. Instrumentally, supercritical fluid extraction can use many of the components of a supercritical fluid chromatographic system. It can be used either as an online sample introduction method for a chromatographic separation or as an offline sample preparation method.

3.2.8 Coupled SuperCritical Fluid Extraction—Supercritical Fluid Chromatography

In this system a sample is extracted with a supercritical fluid, which then places the extracted material in the inlet port of a supercritical fluid chromatographic system. The extract is then chromatographed directly using a supercritical fluid.

3.2.9 Cosolvent (Modifier)

Organic solvents that are used in small quantities in many SFE procedures have become apparent as the technique has matured. These cosolvents are generally used to increase the solubility of the analyte or possibly to increase the separation of co-extractives. Cosolvents such as ethanol have been used to increase the solubility of phospholipids in supercritical carbon dioxide (SCCO₂) [1,2]. Performing SFE with cosolvents usually results in a higher weight percent of fat over that recorded with pure CO₂.

3.3 SuperCritical Fluids

3.3.1 Background and Historical Perspective

In 1822, Baron Charles Cagniard de la Tour discovered the critical point of a substance in his famous cannon barrel experiments. Listening to discontinuities in the sound of a rolling flint ball in a sealed cannon filled with fluids at various temperatures, he observed the critical temperature. Above this temperature, the densities of the liquid and gas phases become equal and the distinction between them disappears, resulting in a single supercritical fluid phase. Although their unique solvent properties were first reported over 100 years ago, only about 20 years ago did supercritical fluids enter the contemporary technical and industrial scene, with the simultaneous appearance in chemical and engineering journals of reports about applications in decaffeinating coffee and tea, extracting hops flavors used in brewing, and extracting aromas and flavors from spices and herbs; by the early 1980s several huge plants (tens to hundreds of millions of pounds per year) were operating in Europe, United States, and Japan. In the intervening years, supercritical fluids have been applied in the development of new or improved products achieving specifications that cannot be met by other industrial processing methods. In Table 3.1, the critical properties are shown for some components, which are commonly used as supercritical fluids.

Supercritical fluid extraction utilizes the ability of certain chemicals to become excellent solvents for certain solutes under a combination of temperature and pressure [3,4]. The term supercritical fluid describes a gas or liquid at conditions above its critical temperature and pressure, i.e., above the critical point.

3.3.2 Basic Properties and Fundamentals of Supercritical Fluids

Two researchers, Hannay and Hogarth, at a meeting of the Royal Society (London) in 1879, reported that supercritical fluids have a pressure-dependent dissolving power—the higher the pressure, the higher their dissolving power [5]. They described their work and summarized their findings as follows: “We have the phenomenon of a solid dissolving in a gas, and when the solid is precipitated by reducing the pressure, it is brought down as a ‘snow’ in the gas.” The researchers
referred to supercritical fluids as gases, which, in fact, they are. In the interest of brevity, the term “gas,” or the abbreviation “SCF” for supercritical fluids, will be used liberally throughout this chapter. The solubility behavior was not exploited until many, many years later, but it is of historical interest to relate some of the events surrounding their findings. There arose serious (but, as were the times, polite) controversy at the October 1879 society meeting. Some of the members who were present said, “Gases cannot dissolve solid compounds. The researchers must have erred and instead found solubility in superheated liquids.” In other carefully planned and executed experiments, the researchers did, however, substantiate their previous findings. Gases, in other words, SCF, could indeed dissolve many compounds.

### 3.3.2.1 Phase Transitions

Figure 3.1 shows isotherms and typical behavior of a real gas as it is subjected to different pressures and temperatures. It should be noted that there are no phase transitions above $T_c$. The isotherms

![Phase diagram for a typical real gas.](FIGURE 3.1 (See color insert following page 240.) Phase diagram for a typical real gas.)
shown in the figure are smooth; they have no tie lines. Tie lines are the horizontal portions of the isotherms, though these are really not really part of the isotherms.

In addition, Figure 3.2 shows three photos of the same system. From left to right, the temperature is increasing. In the upper-left photo, there are two phases present, liquid and gas, and the distinction between them is obvious. The following are near the critical temperature, so the separation of the two phases is becoming obscured. In the photo on the bottom-right, there is no phase distinction, so this is above the critical temperature and is a supercritical fluid as it is also shown in Figure 3.3.

### 3.3.2.2 Phase Behavior

The observations can be explained by looking at the phase diagram of a pure component, e.g., carbon dioxide. Carbon dioxide was substituted for organic solvents (hexane, benzene, carbon tetrachloride, methylene chloride, methanol, and acetone) used in conventional extraction methods. CO₂ is probably the most studied SCF as it is nonflammable, harmless, noncorrosive, inexpensive, and nontoxic, and it can be obtained with high purity [6]. In the case of carbon dioxide, the critical
CO₂ is the solvent of choice for use in SFE because it is "GRAS"—nonflammable, noncorrosive, and inexpensive. In addition, CO₂ has a low critical temperature, which can help prevent thermal degradation of food components when they are being extracted. In Figures 3.4 and 3.5, two projections of the phase diagram of carbon dioxide are shown. Drawing from physical chemistry texts, the critical point is located at the end of the vapor pressure curve, and Figure 3.4 shows a generalized vapor pressure curve and its end. The accented region in the figure denotes the supercritical fluid space where many gases exhibit the propensity to dissolve materials.

In the pressure-temperature phase diagram, the boiling line, which separates the vapor and liquid region and ends in the critical point, is observed. At the critical point, the densities of the equilibrium liquid-phase and the saturated vapor-phases become equal, resulting in the formation of a single supercritical phase. This can be observed in the density-pressure phase diagram for carbon dioxide, as shown in Figure 3.5, where the critical point is located at 304.1 K and 7.38 MPa (73.8 bar). With increasing temperatures, the liquid-vapor density gap decreases, up to the critical
温度，其中连续性消失。因此，高于临界温度，气体不能被液化通过压力。

根据定义，超临界流体是两种物态的物质上临界温度和压力的。在实际意义上，超临界流体在加工和分离方面的用途是有限的，因为它们靠近临界点，其物理性质会发生剧烈变化。这些变化在临界点附近不受密度的限制。许多其他物理性质也随压力变高而发生变化，例如，粘度、相对电导率，以及溶剂强度，这些在密度上相关。在高温下，液体开始像气体一样行为，如图3.5所示。二氧化碳在400 K时，密度线几乎与压力成线性关系 [3]。

在简短的解释中，超临界流体表现出压力依赖的溶解性，溶解的越高，压力的越高，这类物态的溶解性，且这种性质能够被应用于纯化、提取、精制和结晶化。与重要性质相关，压力依赖的溶解性在图3.6中被表示出来，该图展示了在SCCO\textsubscript{2}中，萘在临界点附近溶解度的图示。在压力低于二氧化碳临界压力时，萘的溶解度并没有明显的限制，但是当压力升高时，溶解度逐渐增加至相当高的水平。

萘的溶解度研究至少可以追溯到1870年，德国化学家Büchner，诺贝尔奖获得者，是第一个研究萘在SCCO\textsubscript{2}中的溶解度的人 [7]。《皇家学会的 Proceedings of the Royal Society》和其他期刊描述了在更早期的超临界流体工作，萘的研究仍然在今天为研究者展示了新发现的领域。

### 3.3.2.3 溶剂强度

超临界流体的密度随温度和压力变化，高于临界点时会变化。超临界流体的密度比有机液体的密度高得多，但是固体的溶解度可以比超临界流体的密度高3-10个数量级。1870年在研究碘化钾-乙醇的溶剂时发现了溶剂的溶解度。溶剂强度是超临界流体的性质，可以通过溶解度参数d来表示，d是体态的相似度的平方根。一个溶剂参数表示二氧化碳的溶解度，而粘度随压力变化的模式可以拟合到密度-压力关系。这证实了溶剂强度的超临界流体直接与流体密度相关。因此，固体的溶解度可以通过在温度和压力上做出微小变化来实现。
Another attractive feature of supercritical fluids is that the properties lie between that of gases and liquids. A supercritical fluid has densities similar to that of liquids, while the viscosities and diffusivities are closer to that of gases. Thus, a supercritical fluid can diffuse faster in a solid matrix than a liquid, yet possess a solvent strength to extract the solute from the solid matrix [9].

3.3.2.4 Dispersions in Supercritical Fluids

The ability to design surfactants for the interface between water (or organics) and supercritical fluids offers new avenues in protein and polymer chemistry, separation science, reaction engineering, waste minimization, and treatment. Surfactant design, which is reasonably well understood for conventional reverse micelles and water-in-oil microemulsions for alkane solvents, is more difficult for carbon dioxide because the properties of carbon dioxide are much different from those of water or nonpolar organic solvents [10]. Carbon dioxide has no dipole moment and weaker van der Waals forces than hydrocarbon solvents. It is possible, however, to form dispersions of either hydrophilic or lipophilic phases in a carbon dioxide continuous phase. Organic-in-carbon dioxide dispersions may be stabilized using surfactants like fluorinated compounds, which are carbon dioxide-phobic.

3.3.2.5 Solubility in Supercritical Fluids

According to the ideal gas law, solubility ($\gamma$) is the ratio of vapor pressure ($p_v$) to total pressure ($p_t$) in an SCF; however, the behavior is nonideal and the solubility raises several orders of magnitude. The reason for this increase in the solubility is due to the increase in the density of the SCF. Increase in solubility is defined by the enhancement factor ($E$) that is merely the ratio of actual solubility to the solubility predicted by the ideal gas law.

$$ (E) = \frac{\gamma p_t}{p_v} \quad (3.3) $$

Solubility for a given solute also depends on the SCF itself. Different supercritical fluids have different solubilizing efficiencies. This difference arises due to various intermolecular interactions occurring between the solvent and the solute, which can be explained by the solvent polarity. Here the “like dissolves like” rule applies. Thus, a polar solvent is expected to dissolve a polar solute more efficiently than a nonpolar one. Similarly, the structure similarity of both the solvent and solute plays role in the solubility efficiency.

As an example from typical basic applications, as expressed in previous parts, the solubility of naphthalene in SCCO$_2$ is shown in Figure 3.6. As one would expect, at low pressure its solubility is essentially nil. As the pressure of the gas is increased to above the critical pressure of carbon dioxide (which is 73 atm), the solubility rises, and for many compounds including naphthalene, the rise is often quite dramatic. For example, at 200 atm and 45°C, the solubility is 7%. The solubility behavior shown in Figure 3.6 is the basis of almost all the supercritical fluid extraction/separation processes in operation throughout the world: soluble components are extracted from a substrate by a high-pressure gas, and the extracted components that have been dissolved in the gas are precipitated from the gas when the pressure is reduced, for example, across a pressure reduction valve.

The solubility of components in SCFs can be further enhanced by the addition of a substance referred to as an entrainer, or cosolvent. As volatility of this additional component is usually intermediate to that of the SCF and the solute, the addition of cosolvent provides a further dimension to the range of solvent properties in a given system by influencing the chemical nature of the fluid. Cosolvents also provide a mechanism by which the extraction selectivity can be manipulated. The commercial potential of a commercial application of SCF technology can be significantly improved through the use of cosolvents. A factor that must be taken into consideration when using cosolvents, however, is that even the presence of small amounts of an additional component to a primary SCF can change the critical properties of the resulting mixture considerably.
Starting in the 1960s, many research groups, primarily in Europe, and then later in the United States, examined SCFs for developing advanced extraction processes. European researchers emphasized extraction from botanical substrates, for example, spices, herbs, coffee, tea, and so on, using predominantly SCCO₂, and by the 1980s there were several large SCF extraction processes in operation in Germany, the United Kingdom, and the United States, for decaffeinating coffee and tea and extracting flavors and essential oils from hops, spices, and herbs. As an example of size, a coffee decaffeination plant in Bremen processes more than 60,000,000 kg/year.

The major motivation for developing these SCF processes was the elimination of residual solvents in the products, especially methylene chloride, which had been previously used to decaffeinate coffee. Solvent residues in pharmaceutical and food products were becoming the focus of regulatory attention in the 1970s, and today increasing regulatory attention is being directed to solvent residues. Besides the elimination of solvent residues, there are also other advantages that accrue from employing supercritical fluids in coffee, spices, and herbs, i.e., enhanced flavor and aroma characteristics that cannot be obtained by the traditional organic solvent extraction processes.

Besides the enhanced flavor characteristics and frequently higher yields associated with SFE, some other technical and economic advantages reside in the use of carbon dioxide for the extraction of hop flavors. Organic solvents such as methylene chloride or hexane have previously been the solvents used for the extraction of hops [8]. To obtain the concentrated flavors, it was necessary to distill the organic solvents, and some of the top note aromas are lost during this step. Carbon dioxide produces a superior product because the top notes are not distilled off, and, as mentioned above, the issue of solvent residues, which is a constant spectre, is eliminated by the use of carbon dioxide.

### 3.3.2.6 Extraction with Supercritical Fluids

The SFE has been applied only recently to sample preparation on an analytical scale. With advances in process, equipment, and product design, and realization of the potentially profitable opportunities in the production of high value-added products, industries are becoming more and more interested in supercritical fluid technology [11]. The extraction is carried out in high-pressure equipment in a batch or continuous manner as depicted in Figures 3.7 and 3.8, respectively. In both cases, the supercritical solvent is put in contact with the material from which a desirable product is to be separated.

Supercritical extraction has been applied to a large number of solid matrices. The desired product can be either the extract or the extracted solid itself. This technique resembles Soxhlet extraction except that the solvent used is a supercritical fluid, a substance above its critical

![FIGURE 3.7 Schematic diagram of an SCF batch extraction.](image)
temperature and pressure. This fluid provides a broad range of useful properties [12]. The advantage of using supercritical fluids in extraction is the ease of separation of the extracted solute from the supercritical fluid solvent by simple expansion. In addition, supercritical fluids have liquid-like densities but superior mass transfer characteristics compared to liquid solvents due to their high diffusion and very low surface tension that enables easy penetration into the porous structure of the solid matrix to release the solute. SFE is a relatively new technique in the field of analytical chemistry, having evolved in the last decade as an alternative method of preparing samples before analysis. SFE offers to the analyst many advantages that are not inherent in other sample preparation techniques, such as distillation, extraction with liquid solvents, or low resolution liquid chromatography. The most unique property of supercritical fluids for extraction purposes is the ability to adjust their solubilizing power primarily via mechanical compression (and additionally via temperature), thereby providing the possibility of using one supercritical fluid to extract a host of analytes of varying polarity and molecular size [13]. In addition, solute–fluid binary diffusion coefficients are much greater in supercritical fluid media than in liquid–liquid systems, thereby facilitating fast extraction from a variety of sample matrices.

Furthermore, several legislative protocols (such as the EPA Pollution Prevention Act in the USA) have focused on advocating a reduction in the use of organic solvents, which could be harmful to the environment. The proper choice of supercritical fluid can also provide specific advantages when applied in sample workup before analysis. In addition, the extraction rates are enhanced and less degradation of solutes occurs. Several studies have shown that SFE is a replacement method for traditional gravimetric techniques. In addition, carbon dioxide, which is the most adopted supercritical fluid, has low cost, is a nonflammable compound and devoid of oxygen, thus protecting lipid samples against any oxidative degradation. For example, the low critical temperature of supercritical CO₂ makes it an excellent candidate for extracting thermally labile compounds under conditions slightly above room temperature. In addition, CO₂ provides an extraction environment free from molecular oxygen, thereby limiting potential oxidation of the extracted solutes. Supercritical CO₂, unlike many liquid extraction solvents, is a nontoxic extraction medium; hence, its use in a laboratory environment can eliminate the cost and problems associated with solvent disposal as well as long-term exposure of laboratory personnel to potential toxic vapors.

In practice, SFE can provide appreciable savings in time and cost associated with sample preparation. In general, large polar compounds exhibit almost no solubility in supercritical CO₂,
making it an excellent extraction medium for the separation of nonpolar to moderately polar solutes from such matrices as inorganic solids. However, the solubility of polar analytes can be enhanced in many supercritical fluids by the addition of cosolvents, or modifiers, at low levels to the dense gaseous-phase. By far, the most widely used extraction fluid has been supercritical CO$_2$; however, the extractability of polar solutes can be improved by using a more polar supercritical fluid. Taking CO$_2$ into consideration, the problem with most of the fluids besides CO$_2$ is that these are either difficult to handle or obtain in a pure form.

The following are the advantages of SFEs:

1. Supercritical fluids have a higher diffusion coefficient and lower viscosity than liquids.
2. Absence of surface tension allows for their rapid penetration into the pores of heterogeneous matrices, which helps enhance extraction efficiencies.
3. Selectivity during extraction may be manipulated by varying the conditions of temperature and pressure affecting the solubility of the various components in the supercritical fluid.
4. Supercritical fluid extraction does not leave a chemical residue.
5. Supercritical fluid extractions can use carbon dioxide gas, which can be recycled and used again as part of the unit operation.

Supercritical carbon dioxide has been researched for potential applications in many different fields including food/agriculture, analytical/supercritical fluid chromatography, and the petrochemical/chemical industries.

Many of the supercritical fluids would not be suitable for practical extractions due to their unfavorable physical properties, costs, or reactivities. For example, ethylene, which exhibits a subambient critical temperature, has been widely investigated in the laboratory as an extractant. However, its flammability limits its application in many analytical problems. Conversely, most polar fluids have high critical temperatures, which can prove destructive to both the analyte and the extraction system. Other fluids, like fluoroform, are unique in their ability to solubilize basic solutes through intermolecular hydrogen bonding in the supercritical fluid state, but the exorbitant cost of the fluid limits its use for SFE. It is useful to compare the physical properties exhibited by CO$_2$, under SFE conditions to those associated with liquid solvents under ambient conditions to gain a better understanding of the advantages, which are attendant to conducting extractions in the supercritical fluid state. Table 3.2 compares the physical properties of CO$_2$ under typical SFE conditions with parameters calculated for three liquid solvents: n-hexane, methylene chloride, and methanol at ambient conditions. The density of CO$_2$ at the above conditions is greater than the corresponding value for n-hexane, but lower than the densities exhibited by methanol or methylene chloride. Although density is only an approximate measure of

| TABLE 3.2 | Comparison of Physical Properties of Supercritical CO$_2$ with Liquid Solvents at 25°C |
|----------------|---------------------------------|----------------|----------------|----------------|
|               | CO$_2$                          | n-Hexane        | Methylene Chloride | Methanol |
| Density (g/mL) | 0.746                          | 0.660           | 1.326           | 0.791   |
| Kinematic viscosity (m$^2$/s $\times 10^7$) | 1.00                           | 4.45            | 3.09            | 6.91    |
| Diffusivity of benzoic acid (m$^2$/s $\times 10^9$) | 6.0                            | 4.0             | 2.9  | 1.8    |
| $\left(\frac{P_{sat\ solvent}}{P_{sat\ solute}}\right)$ $^b$ | $1.4 \times 10^5$ | $4.2 \times 10^2$ | $1.2 \times 10^3$ | $3.6 \times 10^2$ |

$^a$ At 200 atm and 55°C.

$^b$ Solute is phenol at 25°C.
intermolecular attraction, the value for CO$_2$ suggests that near liquid-like densities can be achieved for this gas in its supercritical fluid state. Likewise, kinetic-based properties such as viscosity and solute diffusivity, for CO$_2$, have values that are more typical of gases than those of the liquid state. These gas-like transport parameters contribute to improved rates of mass transfer for solutes in supercritical fluid media, resulting in faster extraction. The ratio of the saturated vapor pressures of the extraction solvents to that exhibited by a typical solute, phenol, at 25°C is also tabulated in Table 3.2.

3.4 SUPERCritical FLUID EXTRACTION MECHANISM

Liquid-solid extraction techniques are widely used for isolation of analytes from a solid matrix. One such technique, solid extraction, involves repeated solvent distillation through a solid sample to remove the analyte of interest. This technique is often used for extracting additives from polymers and organics from soils. Not only does Soxhlet extraction requires the use of an organic solvent that will eventually require disposal but also the technique is sometimes very slow. A relatively new extraction technique for isolation of analytes from solid samples is SFE. It has been considered in some studies that SFE collects great attention and interest because of providing short sample preparation time and being better than the conventional extraction techniques [14].

Extraction of soluble species (solutes) from solid matrices takes place through four different mechanisms:

- If there are no interactions between the solute and the solid phase, the process is simple dissolution of the solute in a suitable solvent that does not dissolve the solid matrix.
- If there are interactions between the solid and the solute, then the extraction process is termed as desorption and the adsorption isotherm of the solute on the solid in presence of the solvent determines the equilibrium. Most solids extraction processes, such as activated carbon regeneration, fall in this category.
- Third mechanism is swelling of the solid phase by the solvent accompanied by extraction of the entrapped solute through the first two mechanisms, such as extraction of pigments or residual solvents from polymeric matrices.
- Fourth mechanism is reactive extraction where the insoluble solute reacts with the solvent and the reaction products are soluble hence extractable, such as extraction of lignin from cellulose. Extraction is always followed by another separation process where the extracted solute is separated from the solvent.

Another important aspect in supercritical extraction relates to solvent/solute interactions. Normally, the interactions between the solid and the solute determine the ease of extraction, i.e., the strength of the adsorption isotherm is determined by interactions between the adsorbent and the adsorbate. However, when supercritical fluids are used, interactions between the solvent and the solute affect the adsorption characteristics due to large negative partial molar volumes and partial molar enthalpies in supercritical fluids.

The thermodynamic parameters that govern the extraction are found to be temperature, pressure, the adsorption equilibrium constant, and the solubility of the organic in supercritical fluid [9]. Similar to the retrograde behavior of solubility in supercritical fluids, the adsorption equilibrium constants can either decrease or increase for an increase in temperature at isobaric conditions. This is primarily due to the large negative partial molar properties of the supercritical fluids. In addition to the above factors, the rate parameters like the external mass transfer resistances, the axial dispersion in the fluid phase, and the effective diffusion of the organics in the pores also play a crucial role in the desorption process. A thorough understanding of these governing parameters is important in the modeling of SFE process and in the design, development, and future scale-up of the process.
3.5 SUPercritical fluid extraction theory

In an effort to understand the parameters influencing SFE on the analytical scale, many researchers have studied the thermodynamics of solubility in SCFs and extended this knowledge to supercritical fluid extraction (SCFE) models. There has been a wealth of information relating to SCFE in the chemical engineering and physical chemistry literature. Many simple and relatively fast liquid solvent extraction techniques exist, and when such extractions can be conveniently performed, are quantitative, and do not require concentration for the determination of target analytes, SCFE has few apparent advantages other than the reducing solvent usage.

The density of SCF and the Hildebrand solubility parameter ($\delta$) increases with increasing pressure. The following semiempirical relationship is defined relating the Hildebrand solubility parameter to the density of an SCF:

$$\delta = 0.47P_c^{1/2}\rho$$

(3.4)

Here, $\rho$ is the density of the SCF, which is related to pressure and temperature. The equation is used to calculate the Hildebrand solubility parameter for various SCFs.

The same procedure is used to calculate the Hildebrand solubility parameter for binary fluids. However, the relationship between the solvent strength of a mixed SCF and its density is no longer valid for binary fluids that contain a polar component (modifier). Hildebrand solubility parameters are fairly good predictors of extraction efficiency if the sample matrix has no strong adsorption sites. However, if polar analytes are adsorbed onto a polar sample matrix with relatively strong adsorption sites, small amounts of polar modifier will greatly enhance their desorption. Recovery is vastly improved as compared to the use of pure, unmodified SCF.

The effect of temperature on the solid solubility is different at pressures in the critical range or when the system pressure exceeds the critical value by a factor of two or more. Near the system critical pressure, the fluid density is very sensitive to temperature. Therefore, a moderate increase in temperature leads to a large decrease in fluid density with the consequent reduction in solid solubility. At pressures well above the SCF critical pressure, the solute solubility isotherms exhibit a maximum. It was shown that the maximum is achieved when the partial molar volume of the solute in the fluid phase is equal to the solute solid molar volume [15]. A quantitative correlation and prediction of the solubility of a pure solid in a supercritical gas are possible if the fugacity coefficient of the solid in the gas phase can be obtained from an equation of state.

3.6 EXPERIMENTAL CONSIDERATIONS

The extraction concept is not difficult and complex to perform. The process is simple, with the major process parameters being temperature, pressure, and flow rate of the supercritical fluid. Figure 3.9 presents a basic flow diagram for SFE. Mainly, to obtain the desired pressure value, a pump is used and the extraction fluid is supplied to the extraction cell that is placed in an electric oven. The temperature is kept in a value above the critical temperature of SCF. In this case, the supercritical solvent is put into contact with the material from which a desirable product is to be separated. During SFE, the supercritical solvent, saturated with the extracted compound, is expanded to the atmospheric conditions and the solubilized product is recovered in the separation vessel permitting the recycle of the supercritical solvent for further use [16]. A schematic diagram for a typical SFE system is illustrated in Figure 3.10.

The system is basically formed of a liquid CO$_2$ cylinder, a pump which is preferred mostly to be of syringe type to keep the pressure at an adjusted value [17]. The pressure is kept above the critical pressure and the temperature of the extraction vessel is controlled in supercritical conditions. The extraction process takes place in extraction vessel. After extraction, SCF is passed at a lower pressure and goes through the receiver. CO$_2$, containing droplets and dissolved substances, leaving the receiver is passed through a demister and a carbon scrubber before being recycled to the
liquefaction unit [9]. As a following step, separation of desired component from the stream by SFE can be achieved in different ways. One way is to precipitate the solute from the solvent by reduction of the solvent density that is done by reduction in pressure, increase in temperature, or mixing the extract with atmospheric gases like Ar or N\textsubscript{2}. Sometimes, the product is recovered from the extract by washing it with a suitable solvent.

One should consider the importance of some parameters such as density, diffusivity, critical temperature, critical pressure, etc. so that the SCF can be chosen carefully to carry out the extraction process efficiently in which the extraction pressure and temperature are kept constant at desired values for desired extraction time of the materials at prepared sample sizes.

---

**FIGURE 3.9** Flow diagram of an SFE system.

**FIGURE 3.10** SFE apparatus.

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3.7 APPLICATIONS AND COMMERCIAL PROCESSES OF SUPERCRITICAL FLUIDS

During the past 20 years, SCF processing has developed from a laboratory scale to commercial processes. Applications of analytical SFE are numerous and continue to focus on fossil fuels and environmental samples, foods, natural products, and polymers. Many of these applications have adopted the advances in SFE previously discussed. In reviewing the SFE application areas, we choose to classify the work by sample type rather than analyte type. The relatively new processes include coffee decaffeination, hops extraction, catalyst regeneration, extraction of organic wastes from water and soil, and SCF chromatography. These applications complement older technologies such as residuum oil supercritical extraction (ROSE) process, propane deasphalting, and reaction processes for the production of polyethylene and primary alcohols in SCF ethylene. Tables 3.3 and 3.4 show a

<table>
<thead>
<tr>
<th>Year</th>
<th>Operator</th>
<th>Country</th>
<th>Target Material</th>
<th>Extractor Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1978</td>
<td>HAG AG</td>
<td>Germany/Bremen</td>
<td>Decaffeine/coffee</td>
<td></td>
</tr>
<tr>
<td>1982</td>
<td>SKW-Trostberg</td>
<td>Germany/Munchsmuster</td>
<td>Hop</td>
<td>6,500 L x 3</td>
</tr>
<tr>
<td>1984</td>
<td>Barth</td>
<td>Germany/Wolnzach</td>
<td>Hop</td>
<td>500 L x 1</td>
</tr>
<tr>
<td>1984</td>
<td>Natal Cane</td>
<td>South Africa/Merebank</td>
<td>Hop, red pepper</td>
<td>1,000 L x 2</td>
</tr>
<tr>
<td>1984</td>
<td>By-Products Ltd.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1984</td>
<td>SKW-Trostberg</td>
<td>Germany/Munchsmuster</td>
<td>Decaffeine/coffee</td>
<td></td>
</tr>
<tr>
<td>1984</td>
<td>MüllerExtract</td>
<td>Germany/Coburg</td>
<td>Coffee</td>
<td>100 L x 4</td>
</tr>
<tr>
<td>1986</td>
<td>SKW-Trostberg</td>
<td>Germany/Trostberg</td>
<td></td>
<td>200 L x 2</td>
</tr>
<tr>
<td>1987</td>
<td>Barth</td>
<td>Germany/Wolnzach</td>
<td>Hop</td>
<td>4,000 L x 4</td>
</tr>
<tr>
<td>1987</td>
<td>Messer</td>
<td>Germany/Krefeld</td>
<td>Hop</td>
<td>200 L x 2</td>
</tr>
<tr>
<td>1988</td>
<td>Griesheim</td>
<td>Germany/Munchsmuster</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1989</td>
<td>SKW-Trostberg</td>
<td>Germany</td>
<td>Decaffeine/tea</td>
<td>3,000 L x 3</td>
</tr>
<tr>
<td>1989</td>
<td>HACO AG</td>
<td>Switzerland/Gumlingen</td>
<td></td>
<td>3,000 L x 3</td>
</tr>
<tr>
<td>1989</td>
<td>FRAVEX</td>
<td>Germany/Rehlingen</td>
<td>Aroma</td>
<td></td>
</tr>
<tr>
<td>1990</td>
<td>Jacobs Suchard</td>
<td>Germany/Bremen</td>
<td>Coffee</td>
<td>360 L x 14</td>
</tr>
<tr>
<td>1990</td>
<td>HAG AG</td>
<td>Germany/Bremen</td>
<td>Decaffeine/coffee</td>
<td>50,000 ton/year</td>
</tr>
<tr>
<td>1990</td>
<td>Raps &amp; Co.</td>
<td>Germany/Kulmbach</td>
<td>Spices</td>
<td>500 L x 3</td>
</tr>
<tr>
<td>1990</td>
<td>SKW-Trostberg</td>
<td>Germany/Trostberg</td>
<td>Various products</td>
<td>200 L x 2</td>
</tr>
<tr>
<td>1990</td>
<td>Barth</td>
<td>Germany/Wolnzach</td>
<td>Various products</td>
<td>1,000 L x 4/4,000 L x 2</td>
</tr>
<tr>
<td>1990</td>
<td>SKW-Trostberg</td>
<td>Italy/Venafro</td>
<td>Decaffeine/coffee</td>
<td>20,000 ton/year</td>
</tr>
<tr>
<td>1991</td>
<td>Barth</td>
<td>Germany/Wolnzach</td>
<td></td>
<td>4,000 L x 2</td>
</tr>
<tr>
<td>1992</td>
<td>SKW-Trostberg</td>
<td>Germany/Trostberg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>Agrisana</td>
<td>Italy/Roseto di gli Abruzzo</td>
<td>Pharmaceuticals</td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>Barth</td>
<td>Germany/Wolnzach</td>
<td></td>
<td>200 L x 2</td>
</tr>
<tr>
<td>1995</td>
<td>CEA</td>
<td>France/Pierrelatte</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>Calchauvet</td>
<td>France/Grasse</td>
<td>Pharmaceuticals</td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>Barth</td>
<td>Germany/Wolnzach</td>
<td></td>
<td>650 L x 1</td>
</tr>
<tr>
<td>1996</td>
<td>FLAVEX</td>
<td>Germany/Rehlingen</td>
<td>Various products</td>
<td>360 L x 3</td>
</tr>
<tr>
<td>1996</td>
<td>Essences</td>
<td>Italy/San Marzano</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>Arkopharma</td>
<td>France/Carros</td>
<td>Pharmaceuticals</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>—</td>
<td>Switzerland</td>
<td></td>
<td>600 L x 2</td>
</tr>
<tr>
<td>2003</td>
<td>—</td>
<td>France</td>
<td>Pharmaceuticals</td>
<td>100 L x 1</td>
</tr>
<tr>
<td>2004</td>
<td>—</td>
<td>Spain</td>
<td></td>
<td>8,300 L x 3</td>
</tr>
<tr>
<td>2004</td>
<td>—</td>
<td>Great Britain</td>
<td>Pharmaceuticals</td>
<td>100 L x 1</td>
</tr>
</tbody>
</table>
TABLE 3.4
List of Selected SCCO$_2$ Extraction Plants (Oceania, Asia, Africa)

<table>
<thead>
<tr>
<th>Year</th>
<th>Operator</th>
<th>Country</th>
<th>Target Material</th>
<th>Extractor Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>CUB Foster</td>
<td>Australia/Melbourne</td>
<td>Hop</td>
<td>—</td>
</tr>
<tr>
<td>1984</td>
<td>Natel Canes</td>
<td>South Africa/Merebank</td>
<td>Hop, red pepper</td>
<td>1,000 L x 8</td>
</tr>
<tr>
<td>1984</td>
<td>Fuji Flavor</td>
<td>Japan/Kawasaki</td>
<td>Colorats, flavor</td>
<td>300 L x 1</td>
</tr>
<tr>
<td>1986</td>
<td>Fuji Flavor</td>
<td>Japan/Kawasaki</td>
<td>Colorats, flavor</td>
<td>300 L x 1</td>
</tr>
<tr>
<td>1989</td>
<td>Takasago</td>
<td>Japan</td>
<td>Essential oil</td>
<td>420 L x 1</td>
</tr>
<tr>
<td></td>
<td>International</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1994</td>
<td>—</td>
<td>India/Chennai</td>
<td>Spice</td>
<td>300 L x 1</td>
</tr>
<tr>
<td>1994</td>
<td>Nan Fang</td>
<td>China</td>
<td>Aroma</td>
<td>300 L x 2</td>
</tr>
<tr>
<td>1995</td>
<td>Flavex India</td>
<td>India/Mumbai</td>
<td>Spice</td>
<td>100 L x 1</td>
</tr>
<tr>
<td>1995</td>
<td>—</td>
<td>Malaysia</td>
<td>Spice</td>
<td></td>
</tr>
<tr>
<td>1995</td>
<td>IL HWA</td>
<td>Korea</td>
<td>Ginseng</td>
<td>170 L x 1</td>
</tr>
<tr>
<td>1995</td>
<td>—</td>
<td>China</td>
<td>Nutraceuticals</td>
<td>500 L x 2</td>
</tr>
<tr>
<td>1995</td>
<td>KT &amp; G</td>
<td>Korea</td>
<td>Ginseng</td>
<td>100 L x 1</td>
</tr>
<tr>
<td>1996</td>
<td>Novotech Agro</td>
<td>India/Hyderabad</td>
<td>Spice</td>
<td>500 L x 2</td>
</tr>
<tr>
<td>1997</td>
<td>South East Agro</td>
<td>India/Mysore</td>
<td>Spice</td>
<td>200 L x 2</td>
</tr>
<tr>
<td>1998</td>
<td>Guangxia</td>
<td>China</td>
<td>Various products</td>
<td>500 L x 3</td>
</tr>
<tr>
<td>1999</td>
<td>Shaanxi Jia De</td>
<td>China</td>
<td>Various products</td>
<td>500 L x 2</td>
</tr>
<tr>
<td>1999</td>
<td>Agric. Eng. Co</td>
<td>China</td>
<td>Hop</td>
<td>500 L x 2</td>
</tr>
<tr>
<td>2000</td>
<td>RKS Agro-Tech</td>
<td>India/Bangalore</td>
<td>Spice</td>
<td>300 L x 3</td>
</tr>
<tr>
<td>2000</td>
<td>FiveKingCereals</td>
<td>Taiwan</td>
<td>Rice cleansing</td>
<td>5,800 L x 3</td>
</tr>
<tr>
<td>2000</td>
<td>Green Tek21</td>
<td>Korea</td>
<td>Cosmetics</td>
<td>100 L x 1, 50 L x 2</td>
</tr>
<tr>
<td>2001</td>
<td>Mori oil and fat</td>
<td>Japan/Matsusaka</td>
<td>Essential oil</td>
<td>500 L x 1</td>
</tr>
<tr>
<td>2001</td>
<td>Guangxia</td>
<td>China</td>
<td>Various products</td>
<td>3,500 L x 3</td>
</tr>
<tr>
<td></td>
<td>Toothpaste</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>Guangxia</td>
<td>China</td>
<td>Various products</td>
<td>1,500 L x 3</td>
</tr>
<tr>
<td></td>
<td>Toothpaste</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2001</td>
<td>Guangxia</td>
<td>China</td>
<td>Ginseng</td>
<td>360 L x 1</td>
</tr>
<tr>
<td>2001</td>
<td>—</td>
<td>India</td>
<td>Spice</td>
<td>600 L x 3</td>
</tr>
<tr>
<td>2001</td>
<td>—</td>
<td>China</td>
<td>Health care food</td>
<td>1,000 L x 2</td>
</tr>
<tr>
<td>2001</td>
<td>—</td>
<td>New Zealand</td>
<td>Various products</td>
<td>1,000 L x 3</td>
</tr>
<tr>
<td>2002</td>
<td>—</td>
<td>China</td>
<td>Chinese medicine</td>
<td>600 L x 2</td>
</tr>
<tr>
<td>2002</td>
<td>—</td>
<td>China</td>
<td>Chinese medicine</td>
<td>300 L x 2</td>
</tr>
<tr>
<td>2004</td>
<td>UMAX</td>
<td>Korea</td>
<td>Sesame oil</td>
<td>2,400 L x 2</td>
</tr>
<tr>
<td>2004</td>
<td>—</td>
<td>China</td>
<td>Petrochemicals</td>
<td>500 L x 2</td>
</tr>
<tr>
<td>2005</td>
<td>—</td>
<td>China</td>
<td>Foodstuff</td>
<td>3,000 L x 2</td>
</tr>
<tr>
<td>2005</td>
<td>GansuYasheng</td>
<td>China</td>
<td>Various products</td>
<td>200 L x 3</td>
</tr>
<tr>
<td>2006</td>
<td>Jiusan</td>
<td>China</td>
<td>Soy lecithin/variable</td>
<td>1,500 L x 2</td>
</tr>
<tr>
<td></td>
<td>Oil &amp; Fat Co.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>Ottogi</td>
<td>Korea</td>
<td>Sesame oil</td>
<td>2,300 L x 3</td>
</tr>
</tbody>
</table>
A short list of SCF processes that are constructed by several companies and have been taken in operation recently.

The very special physical properties of SCF distinguish it from liquid and gases. An SCF has a liquid-like density but its viscosity is more like that of a gas, resulting in diffusion coefficients that are much higher than those in liquids. Table 3.5 shows a comparison of these characteristics for a gas, liquid, and SCF.

As mentioned earlier, the first paper dealing with the application of SCF dates from 1879. They discussed the ability of an SCF to dissolve low vapor pressure solid materials. Since then, a substantial amount of work has been done by many investigators to understand the basic fundamentals of a fluid in the supercritical region.

### 3.7.1 Pharmaceutical Applications

Supercritical fluid technology (SFT) has been used in many fields for decades, such as the food industry, chemical processing, polymers, textile, forest product industries, and in the cleaning of precision parts other than pharmaceuticals.

Pharmaceutical and toxicological applications of SFE are especially challenging because of the following reasons:

1. Standards for recovery and reproducibility are more rigorous than for environmental applications.
2. Analytes are usually at trace levels and are highly polar.
3. Matrices are exceedingly complex and often possess coextractives.

Conventional pharmaceutical processing involves extensive use of organic solvents as either antisolvents for recrystallizing drugs from solutions, reaction media in the synthesis of drugs, or extracting agents for selectively isolating drugs from solid matrices. A major research focus in this regard has been the investigation of processes in which the traditional solvents are replaced with SCCO₂.

Since the residual solvent present in the extracted material is of critical importance in the pharmaceutical industry, supercritical fluid carbon dioxide has found several applications. In the pharmaceutical field, it has been widely used for the extraction of natural products like aromatic oils and caffeine, etc. Also, the extraction of vitamin E from soybean oil and a purification method for vitamin E have been well studied. Among the reported applications, the formation of drug particles using dense carbon dioxide either as a solvent or nonsolvent and the “clean” synthesis of drug compounds using carbon dioxide as a reaction medium hold immense appeal for large-scale application in the pharmaceutical industry. Newer areas of their application have appeared, such as particle size reduction and designing of novel drug delivery systems [18].

<table>
<thead>
<tr>
<th></th>
<th>Density (kg/m²)</th>
<th>Diffusion Coefficient (m²/s)</th>
<th>Viscosity (Pa s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas (1 bar, 20°C)</td>
<td>0.6–2.0</td>
<td>1–4 × 10⁻⁵</td>
<td>0.01–0.03</td>
</tr>
<tr>
<td>Liquid (20°C)</td>
<td>600–1200</td>
<td>0.2–2 × 10⁻⁹</td>
<td>0.2–3.0</td>
</tr>
<tr>
<td>SCF</td>
<td>200–900</td>
<td>2–7 × 10⁻⁷</td>
<td>0.01–0.09</td>
</tr>
</tbody>
</table>
3.7.2 ENVIRONMENTAL APPLICATIONS

Owing to strict environmental regulations, supercritical fluids are used as replacements for conventional hazardous chemicals such as hexane. At present, an application area of much activity is the environmental remediation and removal of toxic contaminants from soils and industrial waste using supercritical fluids [19]. Also, SFE has been proposed as an alternative technique for activated carbon regeneration. Over 99% of a majority of organics can be removed from contaminated soil. Organics that have been successfully extracted include PAHs, PCBs, DDT, and toxophene. Carbon dioxide has been used with entrainers for the extraction of highly polar compounds. A commercial process to separate oils from refinery sludge and contaminated soil has been developed by CF Systems Corporation, USA. Chelating moieties that dissolve into carbon dioxide have been developed for the extraction of heavy metals from soil.

3.7.3 FOOD APPLICATIONS

The food industry is always looking for the best separation technology to obtain natural compounds of high purity, healthy products of excellent quality with several industrial applications. Research into energetically less costly technologies with respect to the environment is required. A summary of commercial applications and examples of recent developments illustrate the different possibilities that SFE has in industrial food processes.

One of the first commercial applications of SCF technology was the decaffeination of coffee. Initially, green coffee beans are soaked in water to facilitate the extraction process. The wet beans are then contacted with SCCO$_2$, which selectively removes the caffeine. The caffeine-free beans are then roasted causing the release of the aroma components essential to the development of full coffee flavor. These components are unaffected by the extraction process. The caffeine is removed from CO$_2$ by water stripping or adsorption onto activated carbon, after which the solute-free CO$_2$ is recycled.

As a result of the increasing therapeutic role of essential fatty acids, there is considerable economic incentive to develop a process for the extraction of these materials from natural sources such as fish oils. SFE technology has been regarded as an ideal method for this purpose.

Supercritical fluid extraction, especially using CO$_2$, is today a popular technology for rapid, contamination-free extraction in the food and pharmaceutical industries. Table 3.6 summarizes some of the known applications and newer applications of the SFE technique.

<table>
<thead>
<tr>
<th>TABLE 3.6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SFE Applications in Food Products</strong></td>
</tr>
<tr>
<td>Paprika color (oleoresin) extraction from meats and pickles</td>
</tr>
<tr>
<td>Decaffeination of coffee and tea</td>
</tr>
<tr>
<td>Extraction of vegetable oils and fats</td>
</tr>
<tr>
<td>Extraction of herbal medicines</td>
</tr>
<tr>
<td>Flavors, fragrances, aromas, and perfumes</td>
</tr>
<tr>
<td>Food colors from botanicals</td>
</tr>
<tr>
<td>Antioxidants from plant materials</td>
</tr>
<tr>
<td>Denicotinization of tobacco</td>
</tr>
<tr>
<td>Stabilization of fruit juices</td>
</tr>
<tr>
<td>Hops extraction for bitter</td>
</tr>
<tr>
<td>De-oiling of fast foods</td>
</tr>
<tr>
<td>Essential oil extraction</td>
</tr>
<tr>
<td>Thyme oil extraction from meat and pharmaceutical products</td>
</tr>
</tbody>
</table>

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Beyond environmental samples, application of SFE to samples of food interest remains a major emphasis. Several of these applications were comprehensively reviewed. Supercritical fluids have been used to extract a wide range of analytes from botanical samples. These analytes range from essential oils to phytochemicals, and can include lipid extraction. These extracts have been used for analytical, supplementation, and flavor and fragrance purposes. Some companies have even begun to market botanical extracts obtained by supercritical CO₂ extraction.

In case of SFE of lipids, the technique has been utilized to extract lipids from an assortment of matrices. The first guiding principle is the optimization of the solubility of lipids in supercritical CO₂ and the improvement of the fractionation with respect to a particular lipid species. Some of these extractions have been used to analyze the fat content of different food products. Other extractions have been used to obtain pure lipid extracts or to produce products that contain a reduced amount of certain lipids or other compounds such as cholesterol.

The use of SFE for the determination of fats in food products is one of the most prevalent applications in the field. For instance, dairy products have been subjected to SFE to fractionate lipids and isolate vitamins for quantification.

Flavor compounds and other food volatiles are relatively straightforward to extract with SFE. SFE can be favorable due to the temperature and concentration advantages of using CO₂, as well as the selectivity advantages and the ability to directly couple to gas chromatography (GC) analysis.

Just as SFE found utility in the determination of soil-bound pesticides and herbicides, the technique found application in the determination of these same compounds in food products. For example, the SFE of pesticide residues in fruits and vegetables was applied. Because of the inherent water content in produce samples, where pesticides may be found, drying agents become especially important.

As an other example, the use of SCCO₂ as a replacement of hexane in soybean oil extraction is being considered recently. Data on the extraction and oil composition of soybean oil have been described [20]. It was shown that the separation of oil from CO₂-oil stream at 800 bar can be carried out by dropping the pressure by only 150 or 200 bar at 70°C.

### 3.7.4 SUPERCRITICAL FLUID CHROMATOGRAPHY

Supercritical fluid chromatography may be defined as a form of chromatography, i.e., a physical separation method based on the interaction of an analyte in a mobile phase with a stationary phase, in which the mobile phase is subjected to pressures and temperatures near or above the critical point for the purpose of enhancing the mobile-phase solvating power. Typically, one or both parameters (i.e., pressure and temperature) extend into the critical region during a chromatographic run. This definition encompasses other less-defined forms of chromatography such as dense gas chromatography, hyperpressure gas chromatography, and near (or sub-) critical fluid chromatography.

Supercritical fluids can be used as the mobile phase to separate analytes with chromatographic columns. As in SFE, supercritical fluids can have solvating powers similar to organic solvents, but with higher diffusivities, lower viscosity, and lower surface tension. The lower viscosity allows higher flow rates compared to liquid chromatography, and the solvating power can be adjusted by changing the pressure. Gases, supercritical fluids, and liquids have been compared as chromatographic mobile phases, 5–7 and criteria for selecting suitable mobile phases for SFC have been specified. These considerations include (1) critical pressure; (2) critical temperature; (3) dipole moment; (4) chemical interactions with the stationary phase; (5) chemical interactions with the analyte; (6) compatibility with the detection system; (7) compatibility with seals, tubing, and pumps; (8) environmental and safety considerations; (9) cost; and (10) purity.

A major advantage of SFC is that it offers the advantage of liquid-like solubility, with the capability to use a nonselective gas-phase detector such as flame ionization detector. Analytes that cannot be vaporized for analysis by gas chromatography yet have no functional groups for sensitive detection with the usual liquid chromatography detectors can be separated and detected using SFC. Also, compared with high-performance liquid chromatography (HPLC), SFC provides...
rapid separations without the use of organic solvents. With the desire for environmentally conscious technology, the use of organic chemicals as used in HPLC could be reduced with the use of SFC. Because SFC generally uses carbon dioxide collected as a byproduct of other chemical reactions or is collected directly from the atmosphere, it contributes no new chemicals to the environment. In addition, SFC separations can be done faster than HPLC separations because the diffusion of solutes in supercritical fluids is about 10 times greater than that in liquids (and about 3 times less than in gases). This results in a decrease in resistance to mass transfer in the column and allows for fast high-resolution separations. Compared with GC, capillary SFC can provide high-resolution chromatography at much lower temperatures. This allows fast analysis of thermolabile compounds. The advantages of SFC over gas or high-pressure liquid chromatography have been noted for specific types of samples, such as oligomeric polymer mixtures or complex mixtures of oleophilic components that can be readily solubilized in SCCO$_2$ [21,22].

In fact, helium is supercritical in gas chromatography and the mobile phase has essentially no solvating power, this cannot be considered SFC. Furthermore, if one investigates the practical operating conditions of SFC, it will be obvious that many of the chromatographic analyses are started at pressures below the critical pressure, and occasionally at subcritical temperatures. In general, three conditions must be met to truly define SFC:

1. Mobile phase must always be at temperatures and pressures near or above their critical point.
2. Mobile phase must possess solvating power and, thus, be able to contribute to selectivity in the chromatographic process.
3. Mobile phase must be subject to these conditions throughout the full length of the analytical column.

Finally, the coupling of extraction methods or multidimensional systems with SFC is possible, as in other forms of chromatography. SFC can be conveniently divided into two categories based on column type: open tubular and packed. The choice of column type is not only due to the obvious chromatographic differences (e.g., sample capacity, resolving power, etc.) but also due to the differences in column pressure drop and volumetric flow, which impose different constraints upon the system. Of course, it is the nature of the mobile phase which is unique to SFC.

Preparative SFC is used more and more in research and development laboratories and pilot plants of the pharmaceutical and fine chemical industries. SFC is particularly interesting for the purification of

- Chiral compounds
- Actives or intermediates from complex mixtures
- Lipophilic compounds

Because of the low viscosity and high diffusivity of the SCCO$_2$, preparative SFC ensures faster purification than traditional preparative HPLC. The principle is illustrated in Figure 3.11.

A supercritical fluid chromatograph consists of a gas supply, usually CO$_2$, a pump, the column in a thermostat-controlled oven, a restrictor to maintain the high pressure in the column, and a detector. The column is usually a capillary GC column, but packed LC columns can also be used. The FID is the most common detector, but other GC or LC detectors can also be used. Overall, the equipment is similar to an HPLC device. Major differences over GC and HPLC are its ability to modify pressure or solvent nature during a run.

As an operational principle, cold liquid CO$_2$ is pumped. The pressurized carrier gas enters into a capillary column, which is coated by an adsorbing material, or packed with coated beads, the stationary phase. As the supercritical solution moves through the column, the more strongly adsorbing solutes will be retarded by the stationary phase. On the other hand, larger molecules
cannot sample the lower carrier speeds in boundary regions and thus move faster than small molecules [19]. Before entering the column, it is heated and becomes supercritical. Because of its low viscosity, the pressure at the column outlet is almost identical to the pressure at the column inlet. At the column outlet, the mobile phase is decompressed and heated and becomes gaseous. Products are recovered in cyclones of appropriate design. The gaseous CO₂ is then cleaned and cooled down and returned to the tank following the pathway given in Figure 3.12.

3.8 INSTRUMENTATION

Supercritical fluid extraction was the first application of supercritical fluids. In other words, it can be expressed as the technique of supercritical fluid extraction (SCFE or SFE) that is a new type of green-extracting technique, which is becoming popular in the modern world with wide adaptability and is receiving considerable attention as a method having several kinds of application areas. With this technique, no chemical agent is needed during the process of extraction and the separated substances are also not polluted. Thus, it entirely meets the green requirement of the human race to food, medicine, health protection goods, and cosmetics. The process is the latest technique used to extract oils from natural products, organic pollutants from wastewater, aromatic isomers from

FIGURE 3.11 Picture of SCF chromatograph.
mixtures, low molecular weight materials from polymers, and light components from coal. Also, this technique boasts the features of high extraction effect, high quality, low extraction temperature, low energy consumption, and no pollution, and is especially suitable for the extraction of heat-sensitive and active substances.

FIGURE 3.12 SCF chromatograph.

FIGURE 3.13 SCF extractor.
As an overall technical approach, a supercritical fluid extractor consists of a tank of the mobile phase, usually CO₂, a pump to pressurize the gas, an oven containing the extraction vessel, a restrictor to maintain a high pressure in the extraction line, and a trapping vessel as depicted generally in Figures 3.13 and 3.14 [23]. In Figure 3.13, the compressor stroke rate of the system above is 58 rpm. The extraction pressure and flow rate are controlled by a back pressure regulator as is the separation pressure. The extractions and separation temperatures are controlled and indicated independently. A second atmospheric separation may be performed in a glass vessel or cold trap before the gas stream passes through the flow rate indicator and flow totalizer and is vented to the atmosphere [24].

Analytes are trapped by letting the solute-containing supercritical fluid decompress into an empty vial, through a solvent, or onto a solid sorbent material. Extractions are done in dynamic, static, or combination modes. In a dynamic extraction, material is fed in continuously by means of a pump. The discharge of the processed material is also continuous.

Shown in Figure 3.15 is a pilot plant for the purification/concentration processing of a crude ethanol solution. In a static mode, loading and discharge of the material are carried out by a high-pressure batch extractor, with the opening and closing of the lid automated and the feeding of the supercritical fluid continuous. Figure 3.16 shows the supercritical fluid batch extraction device and the vessel with its automatically opening and closing lid. Extraction of odorants or colorants and removal of pesticides from ginseng extract or powder can be given as examples for this system. In the combination mode, a static extraction is performed for some period, followed by a dynamic extraction.
It is being carried out with carbon dioxide on a large scale for the decaffeination of green coffee beans and the extraction of hops for beer production. Some plant extracts are also produced and some of these are a source of pharmaceutical substances. For example, taxicins can be extracted from yew leaves and used as precursors for anticancer drugs. Carbon dioxide is widely used because of its environmental friendly nature and in some cases it is modified with other solvents to improve its solvating properties. For example, more polar substances are sometimes extracted with carbon dioxide modified with ethanol.

Several firms are employing the technique in various commercial applications, such as coffee decaffeination or botanical extraction. A sample extraction system is described in Figure 3.17.

Components of this pilot plant scale include extraction vessel, separator, high-pressure pump, and complete recycle capability as depicted in Figure 3.18. Among the available standard systems are a 4 L unit and a process development unit (PDU) with maximum allowable working conditions of 5000 psi (333 bar) at 100°C. For decaffeination applications, this system is also used for...
FIGURE 3.16 SFE device (extraction vessel: 390).

FIGURE 3.17 Botanical products SFE system.
extractions of spice, hops, and vanilla bean; and defatting of cocoa powder. For chemical processing applications, polymerization, specialty oil fractionation, countercurrent wastewater extraction can be given as examples. Purification by removal of lipids, supercritical fluid micronizing, and residual solvent removal are other points of view for various application areas [25].

Another sample for SFE system that is illustrated in Figure 3.19 offers the SFE system as a complete turnkey for extractions up to 9200 psi and separations up to 9200 psi. Gas or fluid from your commercial gas bottle passes through a filter to the compressor.

The advantages of SFE (compared with liquid extraction) are firstly that it is relatively rapid because of the low viscosities and high diffusivities associated with supercritical fluids. The extraction can be selective to some extent, by controlling the density of the medium. Separation

FIGURE 3.18 Multipurpose SFE apparatus.
of the fluid substance from the product is relatively easy and the solvent residues in the product are small and of a being nature. Trial experiments are carried out on pilot scale using a system which is installed to be used for both pure and modified fluids and can recycle the fluid. Figures 3.20 and 3.21 show the various additional SFE commercial scale extraction mechanism equipments [26,27].

3.9 CURRENT TRENDS AND FUTURE EXPECTS OF SUPERCRITICAL FLUIDS

If one have a conclusive look through supercritical fluids from historical point of view, as a starting point for scientific discoveries, critical point was discovered by Baron Charles Cagniard de la Tour in 1822. However, supercritical state was properly described only in the year 1870 by Thomas Andrews, who named the “critical point” for the first time.

At the origin of new processes, during 1920s, application studies were done in petrochemistry fields. During 1960s, natural product extraction with SCCO$_2$ was developed. For innovative industrial applications, SCCO$_2$ found its first industrial application with coffee decaffeination, at
FIGURE 3.20  Tea decaffeination plant (Switzerland). (From Uhde High Pressure Technologies, http://www.uhde.hpt.com/.)

FIGURE 3.21  Sesame seed-oil SFE system (2400 L x 2). (From U-MAX, Inc., http://www.iymax.co.kr/)
the end of 1970s. Hop extraction and tea decaffeination processes were developed during the same time.

Supercritical fluids have also been used as unique solvents in a number of analytical techniques, such as nuclear magnetic resonance spectroscopy and thin-layer chromatography (TLC); chemists, however, normally associate the prefix “supercritical fluid” with chromatographic or extraction methodologies that have been extensively developed during the past 15 years.

During the 1980s, a first strong development step occurred for supercritical technology with the building of huge industrial units dedicated to solid extraction, in Europe, in the United States, and in Australia, and also with the building of first development unit for liquid fractionation. First spice extracts started to be delivered onto the market.

During the 1990s, building of industrial units dedicated to toll extraction and world extension of the technology revealed development of new applications and new markets. Also the “renaissance” of SFC occurred in the mid-1970s, largely as a result of improvements in injection and pumping devices, enhanced column efficiencies, and the refinement of transport mechanisms to deliver the separated solutes to modified gas (CC) and liquid chromatographic (LC) detectors. By contrast, SFE, despite a long history as a physicochemical phenomenon and a recent plethora of applications in chemical engineering, has developed as an analytical technique only since the mid-1980s and is presently in an evolutionary state. The current practice of analytical SFE is divided between offline and online methods, despite their common physicochemical basis. Such definitions refer to the mechanism of conducting the extraction.

Current trends in analytical SFE are diverse and worthy of comment. The recent introduction of instrumentation capable of performing extractions on larger and more representative samples is one current trend. As a result, instrumentation manufacturers have had to consider the design of supercritical fluid delivery systems with respect to higher fluid flow rates and extraction pressures. Likewise, the development of multisample extractors for the simultaneous processing of large numbers of samples has further catalyzed the creation of new instrumentation.

In case of future developments, optimal SFE system has yet to be created. Extraction systems need to be developed that offer the flexibility of operating at both higher and lower pressure ranges. SFE is an excellent technique for examining volatile components because the extractions can be conducted at relatively low temperatures and in a non-oxidative environment. Emergence of novel applications for supercritical fluids occurred from the late 1990s: precision cleaning, aerogels, impregnation, particle generation, microencapsulation, etc. Industrial developments in these fields are presently going on.

Reaction processes such as oxidation with supercritical water (SCOW process) or chemical/biochemical synthesis promise industrial successes. Also to be noticed are the innovative processes using subcritical water for natural products extraction together with SFC. Certainly, SFE is a viable alternative to headspace techniques, which depend on thermal energy to volatilize analytes; hence, the authors can envisage a bright future for SFE in sensory analysis problems.

3.10 CONCLUSION

In the last decade, new trends have emerged in the food industry. These trends include an enhanced concern for the quality and safety of food products, increased preference for natural products over synthetic ones, and broadened regulations related to nutritional and toxicity levels of active ingredients. These trends have driven supercritical fluid technology to become the primary alternative to traditional solvent extraction for the extraction and fractionation of active compounds.

Supercritical fluid extraction is an extraction process using a supercritical fluid as a solvent. SFE utilizes the ability of certain chemicals to become excellent solvents for certain solutes under a combination of temperature and pressure. The physiochemical properties of a fluid in the supercritical state are in between those of a typical gas and liquid. For example, the density of a supercritical fluid can be changed by varying the pressure on the fluid. Carbon dioxide is certainly the most
popular fluid because of its physiological compatibility, nontoxicity, inflammability, easy availability, convenient critical parameters \((T_c = 31{\text{C}}, P_c = 7.38 \text{ MPa})\), inexpensiveness, and environmental friendliness.

Supercritical fluid extraction has proved effective in the separation of essential oils and its derivatives for use in the food, cosmetics, pharmaceutical, and other related industries, producing high-quality essential oils with commercially more satisfactory compositions (lower monoterpenes) than obtained with conventional hydro distillation.

Whether it is used as a solvent for extraction in analytical methods such as gravimetric determination of fat content or in large-scale extractions such as decaffeinating coffee, SCCO\(_2\) has proven its usefulness as a replacement for organic solvents.

Supercritical fluid extraction with CO\(_2\) proved to be highly selective for caffeine, prompting its use as the selected solvent in the commercial decaffeination of coffee and black tea. Recent investigations have demonstrated the potential exploration of solvent and antisolvent properties of carbon dioxide in the recovery of alkaloids such as theophylline, theobromine, and pilocarpine, among others.

Supercritical fluid extraction with CO\(_2\) delivers the most natural-smelling and -tasting extracts because there are no volatiles removed in a residual solvent-removal post-processing step. This has benefits for an array of products. For instance, many spices are known for their therapeutic value. Supercritical fluid technology offers tremendous advantages, such as the absence of any organic solvent residues and selective extraction and fractionation of different compounds. All of these advantages are almost impossible to obtain easily from conventional processes at low operating costs. Therefore, supercritical fluid technology is an ideal tool for the processing of active compounds for use in food products and dietary supplements.

To conclude, with increasing concern about the use of organic solvents and their disposal, SFE is gaining popularity faster than ever before. The future looks promising for the use of supercritical fluids, with new methods of extraction constantly being developed, as with other novel uses for the food processing industry.

REFERENCES
