

STUDY OF SUPERCRITICAL FLUIDS

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INTRODUCTION:

There has been rising concern in recent years over supercritical fluids for organic waste treatment and other applications. The discovery of the presence of critical point dates back to 1822. The temperature and pressure beyond the critical point are in the supercritical state. Critical points are usually at high pressures. Therefore, a high-pressure test facility (high temperature and high pressure depending on the case) is required for a systematic study of fluids in the near- or supercritical state. This might have been the main reason why studies in this field were comparatively few until recently. Research on supercritical fluids and the applications development reached the initial peak during the period from the second half of the 1960s to the 1970s followed by the secondary peak about 15 years later. The initial peak was for the separation and extraction technique as represented by the extraction of caffeine from coffee beans. Since the practical application in Germany in 1978, a number of practical plants have been in operation. The secondary peak concerns decomposition of organic (waste) substances, which started when the U.S. Department of Defense began studies on using supercritical water as a means for completely decomposing chemical weapons. And the tertiary peak is about to come with mounting interest in the possible development of new material program.

WHAT ARE SUPERCRITICAL FLUIDS?

Supercritical fluids are described as “fluids in the temperature and pressure state of over the critical point”. This definition, however, is not sufficient and not providing a good explanation for understanding them. For persons handling them, they are not different from “high-pressure gas.” They are not distinguishable from gas because they are in a non-condensed state, which disables handling without using a sealed container. In other words, they may be considered to be gas that does not transform to the liquid phase with discontinuous change in the density when the pressure rises under a constant temperature. Substances change their phase depending on the balance of forces between the force to form the liquid or solid phase by condensation under inter-molecular attraction and the force to make free thermal movement. At high temperature, however, the force of particles to move about freely exceeds

that of the inter-molecular force if the inter-molecular distance is minimized under pressure. The supercritical state is thus reached where no condensed phase is produced. When the pressure rises, the gas density becomes higher, however. The inter-molecular distance then becomes shorter, making it impossible to disregard the effects of inter-molecular action. In other words, when viewed from the molecules inside or from the microscopic standpoint, they are in a state close to liquid. If the molecular movement can be directly observed, it is assumed to be as violent as in the gaseous state. When observed in a still photograph, it may resemble that of the liquid. This is the reason why “supercritical is the intermediate state between gas and liquid.”

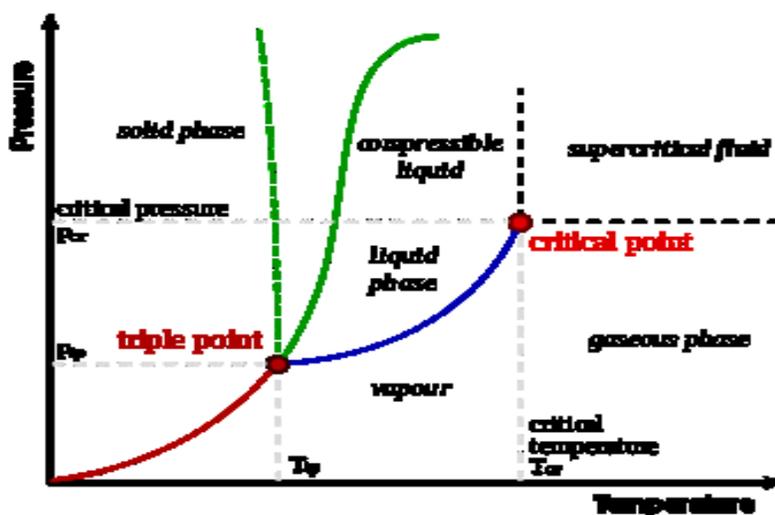


Figure1: critical point diagram

Table 1: Critical points of typical solvents

Compounds	Critical Temperature (°C)	Critical Pressure (atm)	Critical Density (g/ml)
Carbon Dioxide	31.3	72.9	0.448
Ammonia	132.4	112.5	0.235
Water	374.15	218.3	0.315
Nitrous Oxide	36.5	71.7	0.45
Xenon	16.6	57.6	0.118

Krypton	-63.8	54.3	0.091
Methane	-82.1	45.8	0.2
Ethane	32.28	48.1	0.203
Ethylene	9.21	49.7	0.218
Propane	96.67	41.9	0.217
Pentane	196.6	33.3	0.232
Methanol	240.5	78.9	0.272
Ethanol	243.0	63.0	0.276
Isopropanol	235.3	47.0	0.273
Isobutanol	275.0	42.4	0.272
Chlorotrifluoromethane	28.0	38.7	0.579
Monofluoromethane	44.6	58.0	0.3
Cycrohexanol	356.0	38.0	0.273

PROPERTIES OF SCF:

1. Supercritical fluids have highly compressed gases, which combine properties of gases and liquids in an intriguing manner.
2. Supercritical fluids can lead to reactions, which are difficult or even impossible to achieve in conventional solvents.
3. Supercritical fluids have solvent power similar to light hydrocarbons for most of the solutes. However, fluorinated compounds are often more soluble in supercritical CO₂ than in hydrocarbons; this increased solubility is important for polymerization.
4. Solubility increases with increasing density (that is with increasing pressure). Rapid expansion of supercritical solutions leads to precipitation of a finely divided solid. This is a key feature of flow reactors.
5. The fluids are commonly miscible with permanent gases (e.g. N₂ or H₂) and this leads too much higher concentrations of dissolved gases than can be achieved in conventional solvents.
6. In general terms, supercritical fluids have properties between those of a gas and a liquid.

Table 2: Density, diffusivity and viscosity for typical liquids, gases and supercritical fluids

	Density (kg/m ³)	Viscosity (μPa·s)	Diffusivity (mm ² /s)
Gases	1	10	1-10
Supercritical fluids	100-1000	50-100	0.01-0.1
Liquids	1000	500-1000	0.001

ADVANTAGES OF SUPERCRITICAL FLUIDS:

- SCF provide lower operating temperatures.
- SCF gives improved yield.
- SCF gives improved product properties.
- SCF enables favorable combination of process steps.
- Regeneration of the SC solvent is easier.
- SCF gives lower production cost.
- SCF shows high volatility compared to the dissolved substances.
- SCF gives complete separation of solvent from extract and raffinate.

LIMITATIONS OF SUPERCRITICAL FLUIDS:

- SCF require elevated pressures for working.
- SCF have relatively high costs of investment.
- SCF demands unusual operating conditions.
- SCF shows complicated phase behavior.

APPLICATIONS AND COMMERCIAL PROCESSES OF SUPERCRITICAL FLUIDS:

Any commercialization of a process that uses supercritical fluids must involve a cost analysis that should indicate that the advantages in the new process offsets the penalty of high pressure operations. A variety of supercritical fluid processes have been commercialized. Details of a few such processes are given below. Many other processes have been investigated on a lab or pilot plant scale and have the potential to be scaled up in the near future.

1. Supercritical Fluid Chromatography:

Supercritical fluid chromatography is now often used as an analytical tool. The density is used as the controlling feature. Separations are based on a user programmed density profile with the supercritical fluid as the mobile phase. This analytical technique has been successfully used to separate oligomers and high molecular weight polymers. Supercritical fluids are used as the extracting solvents for the removal of

polyaromatic hydrocarbons from soil. It is now a standard method for gas chromatography sample preparation because the extraction is considerably faster than Soxhlet extraction.

2. Fractionation:

Supercritical fluids can be used to fractionate low vapor pressure oils and polymers. This fractionation is difficult to achieve in distillation because the impurities have about the same volatility as the primary components reducing the overall selectivity. Kerr-McGee Inc. has developed a commercial process for the separation of heavy components of crude oil. Fractionation with respect to chemical composition is possible and has been investigated to produce polymer fractions of low polydispersity starting from a parent material of high polydispersity.

3. Reactions:

Supercritical fluids are attractive media for several chemical reactions. The properties of supercritical fluids mentioned earlier can be used to advantage. By small adjustments in pressure, the reaction rate constants can be altered by two orders of magnitude. Equilibrium constants for reversible reactions can also be changed 2-6 fold by small changes in pressure. This dramatic control over the reaction rates has led to the design of several reactions in different areas of biochemistry, polymer chemistry and environmental science. In bioreactions, increased solubilities of hydrophobic material and the potential to integrate the separation and reaction steps has led to research in this area. The use of lipase and synthesis of monodisperse biopolymers holds commercial promise. Carbon dioxide has also been extensively studied for homogeneous polymerization of a few polymers such as fluoroacrylates. The feasibility of free radical polymerization of polystyrene and the polymerization of polyethylene has also been investigated. Carbon dioxide is also often used as a swelling agent for a polymer substrate. Though highly corrosive and a high critical temperature and pressure, supercritical water has been one of the most studied medium for chemical reactions. Supercritical water has the ability to dissolve many nonpolar organic compounds such as alkanes and chlorinated biphenyls and can dissolve in several gases. It is thus an attractive media for oxidative reactions and has been used to treat a wide variety of waste water streams from chemical, petroleum, textile industries. Huntsman Corporation has commercialized a hydrothermal oxidation unit to treat alcohol and amine contaminated water.

4. Applications in the material and polymer industry:

Supercritical fluids are used extensively in the material and polymer industry. Rapid expansion from supercritical solutions across an orifice or nozzle is used commercially to precipitate solids. In this technique, a solute dissolved in supercritical fluid is depressurized rapidly. By controlling the operating

variables carefully, the desired precipitated morphology can be attained. In an another process, called gas anti-solvent, a supercritical fluid is rapidly added to a solution of a crystalline solid dissolved in an organic solvent. Since the solute has limited solubility in the fluid, the supercritical fluid acts as an anti-solvent to precipitate solid crystals. By varying the density of the fluid, the particle size distribution of final crystals can be finely controlled. Another process is the precipitation using a compressed fluid anti-solvent. In this process, the solution is sprayed through a nozzle into a compressed fluid and the solvent diffuses rapidly into the supercritical fluid while the fluid swells the solution to precipitate the solute. This process has been used commercially to form nanometric monodisperse microspheres of polymers. Another process that has been commercialized is the usage of supercritical fluid carbon dioxide to produce foamed parts. Since supercritical fluids depress the glass transition temperature of the polymer, polymer foams can be formed at room temperature by directly adding the supercritical fluid into the extruder.

4. Food applications:

Carbon dioxide is the most common supercritical fluid in the food industry. Due to the non-toxicity and low critical temperature, it can be used to extract thermally labile food components and the product is not contaminated with residual solvent. Further, the extracts color, composition, odor, texture are controllable and extraction by supercritical fluid carbon dioxide retains the aroma of the product. Supercritical carbon dioxide extraction is used as a replacement for hexane in extracting soybean-oil and has been tested for extraction from corn, sunflower and peanuts. Supercritical fluid extraction provides a distinct advantage not only in the replacement but also extracts oils that are lower in iron and free fatty acid. To satisfy the consumer's need for 'lighter' foods, developmental work on supercritical extraction of oils from potato chips and other snack foods are been carried out. In addition, supercritical carbon dioxide has also been used to extract lilac, essential oils, black pepper, nutmeg, vanilla, basil, ginger, chamomile, and cholesterol.

A large amount of research has been concentrated on the decaffeination of coffee by supercritical carbon dioxide. Thus, it is not surprising to note that this was the first process to be commercialized (in 1978), whose primary step is supercritical extraction. Dry carbon dioxide cannot extract caffeine from dry coffee effectively and that the beans should be pre-wetted by water. Soaking of about 2 hours is necessary for efficient extraction of caffeine from coffee beans by supercritical carbon dioxide. Commercial processes for decaffeination of coffee include the Kraft General Foods in USA and several processes in Germany.

5. Pharmaceutical applications:

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. The extraction of vitamin E from soybean oil and a purification method for vitamin E has been well studied. The latter process avoids the step of vacuum distillation, which usually results in the thermal degradation of the product. Solubilities and recrystallization of various drugs has been demonstrated in supercritical fluids.

6. Environmental applications:

Due to strict environmental regulations, supercritical fluids are used as replacements for conventional hazardous chemicals such as hexane. Supercritical fluid extraction has been proposed as an alternative technique for soil remediation and 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.

MAJOR APPLICATIONS OF SCF IN ANALYTICAL CHEMISTRY:

1. Supercritical fluid chromatography

Supercritical fluid chromatography (SFC) is a hybrid of gas and liquid chromatography. SFC is of importance because it permits the separation and determination of a group of compounds that are not conveniently handled by either gas or liquid chromatography. These compounds are either non-volatile or thermally labile so that gas chromatography cannot be used and they do not contain functional groups that make possible detection by liquid chromatography. SFC has been applied to a wide variety of materials including natural products, drugs, foods, pesticides and herbicides, fossil fuels, explosives and propellants.

Supercritical Fluid Chromatography - Instrumentation

A supercritical fluid chromatography instrument consists of a mobile phase container, an injector, a column in an oven, a restrictor and a detector. The components are similar to those of a gas chromatograph with exception of the restrictor. The restrictor is needed to maintain the pressure above the critical point. If the detector is a gas-phase detector working at atmospheric pressure (e.g., Flame Ionization Detector FID) the restrictor is placed before the detector. When using a detector that works under supercritical conditions (e.g., Ultra Violet detector UV) the restrictor is placed after the detector.

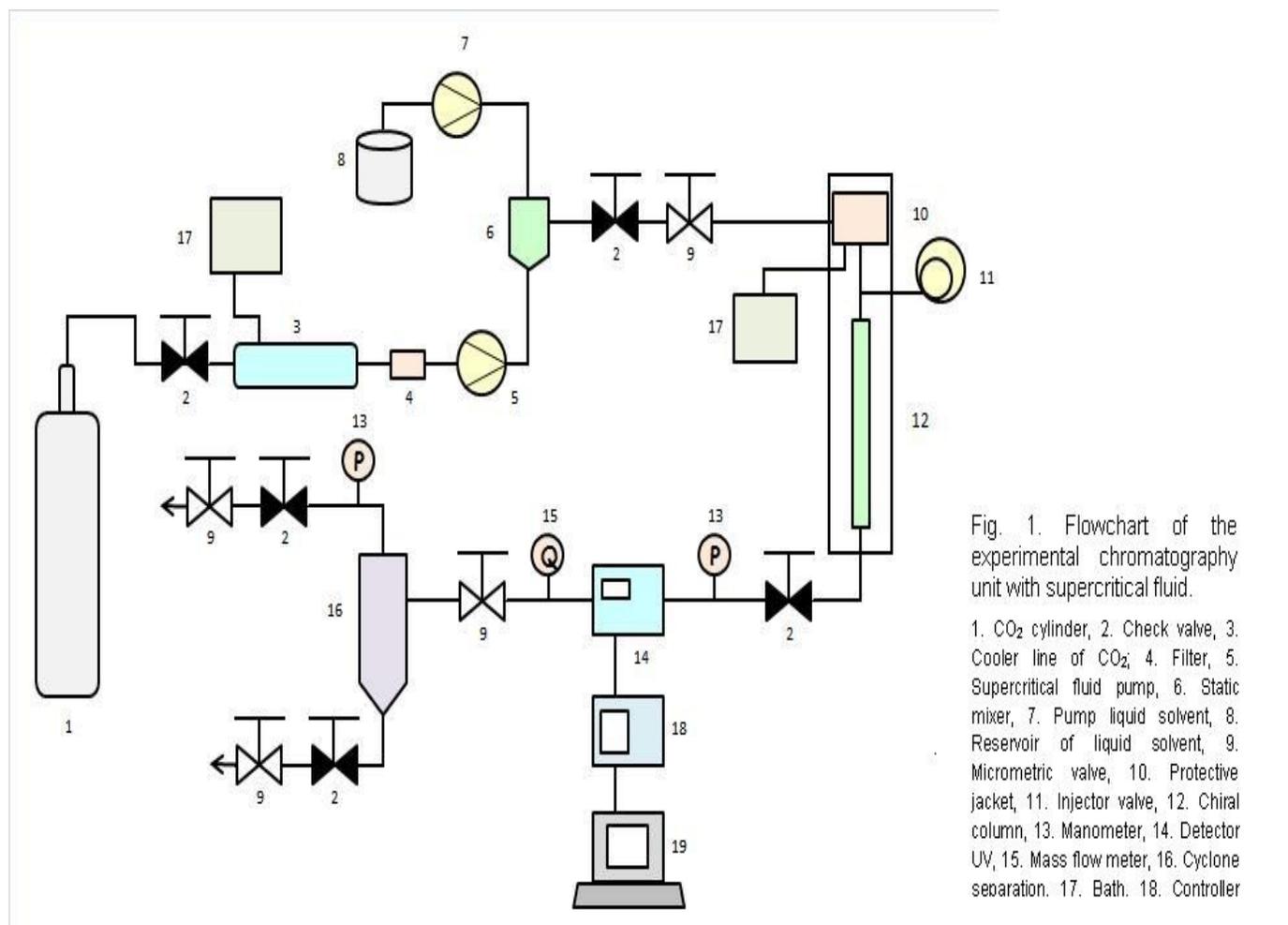


Figure2: Instrumentation of SFC

Mobilephases:

The most widely used mobile phase for supercritical fluid chromatography is carbon dioxide because it is an excellent solvent for a variety of organic molecules. A number of other substances have served as mobile phase including ethane, pentane, nitrous oxide, dichlorofluormethane, diethylether, ammonia and tetrahydrofuran.

Columns:

Both open-tubular and packed columns are used for SFC. The open-tubular columns are most useful for separations requiring high-efficiency separations and for complex samples. Packed columns are most useful for high-speed separations requiring a moderate column efficiency and for samples containing fewer components.

Column Efficiency:

The expanded form of the Golay equation for open tubular columns is given by ,

$$h = \frac{2D_m}{u} + \frac{d_c^2(1 + 6k + 11k^2)u}{96(1 + k)^2D_m} + \frac{2kd_f^2u}{3(1 + k)^2D_s}$$

where h is the plate height, u is the average mobile phase linear velocity along the column, d, is the column internal diameter, k is the capacity factor, df is the stationary phase film thickness, and D, and D, are the solute diffusion coefficients in the mobile and stationary phases, respectively.

Detectors:

When using capillary columns and carbon dioxide practically all Gas Chromatography (GC) detectors and many High Performance Liquid Chromatography (HPLC) detectors can be used. With packed columns and organic modifiers the number of detectors available is more limited. The Flame Ionization Detector (FID) is the most frequently used detector. Other detectors that often are used are Flame Photometric Detector (FPD), Electron Capture Detector ECD and Mass Spectrometer (MS).

General Requirements for Column Technology:

The traditional names that have been adopted for the different packed column types are borrowed from LC. The conventional 4-6-mm i.d. packed column is not the most common dimension of packed columns in SFC as it is in LC. Limitations in volumetric pumping speeds and/or volumetric flow rates for the detectors of choice have helped to make packed columns of micro sizes increasingly common in SFC. The packed capillary column has the advantages of lower volumetric flow rates, making them more compatible with mass flow sensitive detectors; smaller elution peak volumes, which provide greater sensitivity in concentration sensitive detectors; easier sample transfer in multidimensional systems; and higher permeability, which allows the use of longer columns for better resolution. Open tubular columns for SFC are typically 3-10-m x 50-µm i.d., which represents a practical compromise in efficiency and speed. The requirements that must be satisfied by column technology include (1) well-deactivated surfaces and stationary phases, (2) uniform stationary phase films, and (3) well-immobilized stationary phase films. There continues to be a demand for more inert columns, and this demand has resulted in innovations in deactivation procedures for column and support materials. The most deactivated columns have been open tubular columns. This is a result of their low surface area and much lower porosity when compared to silica or alumina packing materials. In addition to causing adsorption of polar analytes, active sites lead to poorly controlled and nonreproducible retention. Active sites generally necessitate the use of polar modifiers. In the packed column, the stationary phase is normally near monomolecular thickness and is polymerized and chemically bonded to the support. Immobilization (generally cross-linking of the

polymeric phase) is an essential ingredient in the preparation of open tubular columns. It must be performed to resist dissolution, but without lowering solute diffusion within the phase.

Packed Column Technology:

Since the early days of SFC, packed column SFC technology has depended on materials available from the current state-of-the-art LC technology. It is not surprising that LC packing materials perform well under SFC conditions, since both techniques depend on the ability of the mobile phase to solvate analyte molecules. Particle sizes referred to in publications normally vary from 3 to 10µm in diameter with pore sizes ranging from 100 to 300 Å, (corresponding to a surface area of ca. 100-300m²/g). Of these, the most commonly used particle size is 5- µm diameter. This particular size is popular because it is small enough to give relatively small plate heights, while being commercially available in sufficient uniformity and narrow distribution to allow efficient packing to be accomplished. Smaller particles provide smaller plate heights; however, they also reduce permeability and increase the pressure drop across the column. The feasibility of working with small diameter particles in SFC has been discussed by several groups

Open Tubular Column Technology:

Open tubular columns for SFC must possess the usual qualities of high efficiency, inertness, and lasting stability, which are characteristic of open tubular columns for GC. The main differences in the preparation of the columns are related to the smaller internal diameters characteristic of SFC columns.

1. SFC vs. HPLC:

According to the intermediate properties of supercritical fluids between those of a gas and a liquid, supercritical fluids appear to be a good solution to avoid problems of both HPLC and GC. Supercritical fluid mobile phases have much greater solubilizing power than gaseous ones and can, therefore, be used for the separation of in volatile and high-molecular-mass samples unsuited to GC. Although the typical solute diffusion coefficient in supercritical fluids is intermediate between those of gas and liquid, it is noteworthy that the diffusion coefficient is an order of magnitude greater than in liquid. This fact has important chromatographic implications concerning separation time and column efficiency. SFC is theoretically up to ten times faster than HPLC, because of the lower viscosity and higher diffusivity in the mobile phase, SFC columns typically provide a three- to five-fold reduction in analysis time over HPLC. Moreover, column equilibration times are far shorter with SFC compared with HPLC, reducing once again overall analysis time. The typical minimum values for height equivalent to a theoretical plate for packed-column SFC (pSFC) and HPLC are very similar, the most important difference, however, is that the minimum value in SFC is achieved at linear velocities three to five times greater than for HPLC. Figure

below shows that the optimal height equivalent to a theoretical plate (HETP) is similar in HPLC and SFC (typically 12 μm) but, in SFC, it is reached at much higher linear velocity (typically 0.1 cm s^{-1} for HPLC and 0.4-0.5 cm s^{-1} for SFC). Further, the low viscosity of supercritical fluids results in lower pressure drops along the column, thus up to ten columns can be assembled, serially, to afford up to 200,000 theoretical plates.

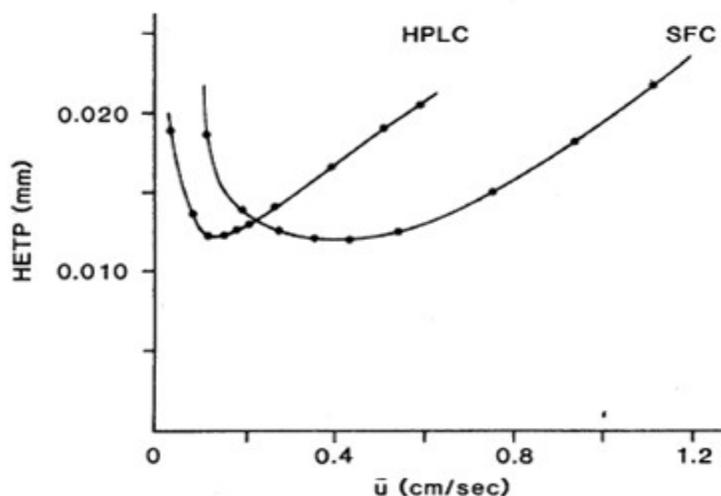


Figure 3: Van Deemter plots for the analysis of pyrene by HPLC and SFC. (HETP is the height equivalent to a theoretical plate, \bar{u} is the linear velocity)

Another important advantage of SFC compared with HPLC is that SFC provides rapid separations without the use of large volumes 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. This is especially true when it comes to preparative scale where large quantities of solvents are involved.

To summarise, SFC possesses a number of advantages when compared to HPLC: shorter analysis time, higher efficiency, fast column equilibration, less harmful and more cost-effective mobile phases, easy to hyphenate with many detectors and easy to scale-up from analytical to preparative scale.

However, SFC and HPLC should not be seen as competitive techniques. HPLC will handle samples that are not suitable for SFC, and the converse is true. The two techniques are actually complementary and being equipped with both types of instruments will provide the analyst with the means to tackle more analytical challenges.

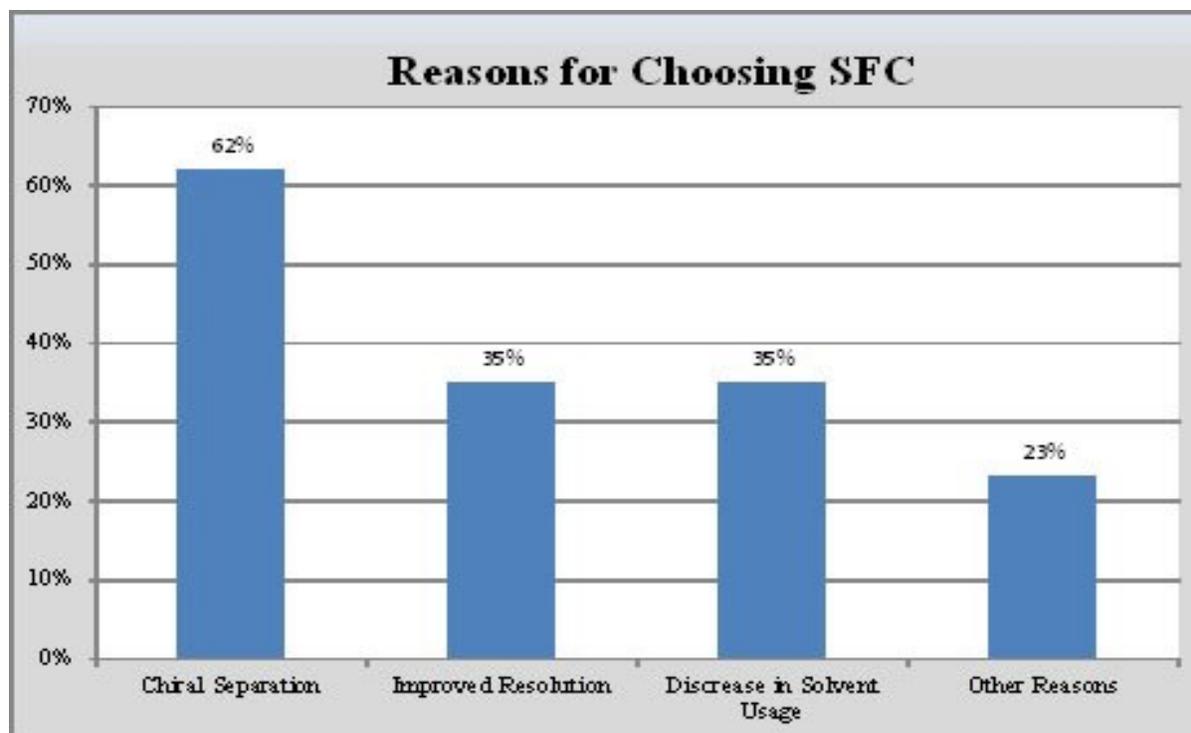


Figure 4: Reasons for choosing SFC

Applications of SFC:

1. Used to analyse and purify chiral compounds.
2. Used in pharmaceutical industries.

2. Supercritical fluid extraction

Principle:

The first guiding principle is the optimization of the solubility of materials to be extracted (lipids, heavy metals, natural products) in supercritical CO₂ and the improvement of the fractionation with respect to a particular lipid species, natural products.

Introduction:

Analytical supercritical fluid extraction (SFE) involves the use of compressed gases, held above their critical temperature (T_c), for the extraction of analytes from a variety of sample matrices. The technique offers some unique advantages over conventional sample preparation techniques, particularly when used as the extraction fluid. As noted in previous sections, the same properties that make supercritical fluids unique mobile phases for SFC, are also responsible for their performance when they are used in the extraction mode. For example, adjustment of the fluid pressure permits, to a degree, the selective extraction of specific analytes for subsequent analysis. Improvements, in the kinetics of extraction are also realized by using supercritical fluids, due to the higher diffusion coefficients exhibited by solutes in the

dense fluid media compared to their diffusivities in liquid-liquid extraction solvents. Recently, supercritical fluids have been cited as excellent extraction solvents, since their use avoids the problem of solvent waste disposal as well as exposure of laboratory personnel to toxic solvents. Chronologically, analytical SFE developed somewhat later than SFC, although Stahl C1453 reported on the coupling of SFE with thin-layer chromatography (TLC) as early as 1976. Supercritical fluid extraction has also been utilized by chemical engineers since the 1970s and the literature in this field contains valuable information for the analytical chemist. Today, analytical SFE is practiced ranging from the submilligram to the 100-g level. Analytical SFE can be performed as an independent sample preparation technique or be coupled “on-line” to such chromatographic methods as GC and SFC. In this section we discuss the fundamental concepts governing this technique, its practice, and a sampling of the applications in which it has been used.

Fundamentals:

Since analytical SFE is often used as an alternative for liquid-liquid extraction, it is useful to compare some of the physicochemical properties of supercritical fluids with those exhibited by typical liquid extraction solvents. It is the ability of supercritical fluids, such as CO₂, to achieve “liquid-like” densities coupled with their “more favorable” transport properties compared to liquid solvents that permit them to achieve higher extraction fluxes than those obtained using liquid solvents. As noted in Section 3, the solubility characteristics of a supercritical fluid are directly related to its density. CO₂, at high densities can have similar solvent properties to such liquids as chloroform and acetone. At intermediate levels of compression, CO₂ and other supercritical fluids can emulate the solvent power of nonpolar hydrocarbons, such as n-pentane or diethyl ether. Such a scale explains the qualitative features of supercritical fluids, but often leaves the impression that it is necessary to match the solubility parameters of the extraction fluid and solute to achieve a successful extraction. Other methods have been developed to assist the analyst in choosing the density or pressure required for dissolving the solute in the supercritical fluid, or to predict the solubility of a solute in the fluid at a specific pressure or temperature. These concepts and the rules formulated by Stahl and co-workers provide guidance in predicting the miscibility and extent of solubilization of a solute in a supercritical fluid.

The Practice of Supercritical Fluid Extraction:

Supercritical fluid extraction has been implemented in the laboratory using a variety of methods and equipment. However, a generic SFE apparatus, usually consists of a pump or compressor, an extraction vessel, a pressure reduction device, followed by a collection vessel. Analytical SFE is usually practiced in

either an off-line or on-line mode. The choice between the two SFE techniques will be dictated by the problem facing the analyst; however, there is some merit in starting with the off-line mode because of its inherent simplicity. In general, off-line SFE permits the processing of larger sample sizes, while sample size in on-line SFE is dictated by the constraints of sample overload on the chromatographic column. On-line SFE is more prone to contamination, but is inherently more sensitive than offline techniques. This makes on-line SFE coupled with SFC or GC an excellent technique for characterizing extremely small samples. A typical off-line SFE apparatus with provision for collecting the extracted analytes in a vial after decompression of the extraction fluid. In this scheme, the extraction fluid is delivered through a pump, whose heads are cooled to a sub-ambient temperature to assure liquefaction of the gas. A second pumping module is also connected in-line to provide for the addition of a modifier (methanol in this case) to the extraction fluid. The extraction vessel is contained in a heater assembly that equilibrates the extraction fluid to the desired temperature. After extraction, the fluid pressure is jettisoned through a back pressure regulator, and the analytes of interest are collected in a solvent laden vial, cooled by the adiabatic, isoenthalpic expansion of the expanded fluid.

Supercritical Fluid Extraction - Instrumentation

The main components of the SFE instrument are a pump, an extraction chamber, a recovery chamber and a collection device. In order to generate a supercritical fluid, carbon dioxide is pressurized above its critical pressure in a pump. The mixture to be separated is placed in the extraction chamber and put in contact with the supercritical fluid. One of the elements (component A) in the mixture dissolves better in the critical fluid and leaves the residue enriched in the other components. The loaded solvent is then transferred to a recovery chamber, where component A is recovered by lowering the solvent's density. This density can be achieved by raising the temperature at constant pressure but more often it is achieved by reducing the pressure at constant temperature. After depressurizing, two methods have been adopted for collection of the extracted analyses, these are on-line or off-line SFE. In on-line SFE, the extracted analytes are direct coupled to a chromatographic separation system such as SFC, gas chromatography (GC) or high performance liquid chromatography (HPLC) with appropriate detection. Directly coupled GC is limited to volatile compounds while SFE-SFC can be used for higher molecular weights. The off-line approach allows the extraction and concentration of analytes for subsequent HPLC analysis.

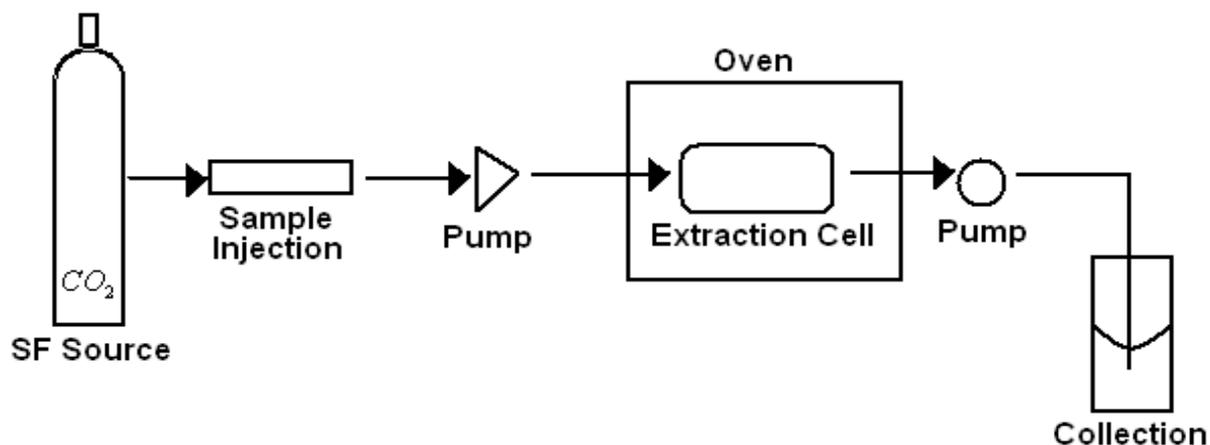


Figure 5: Instrumentation of SCE

Applications of SFE:

1. Application of SFE to enantiomeric separations:

Chiral separation is a very important issue for the pharmaceutical industry. The applicability of SFE as an effective and green technique for enantioseparations is known since the late 1990s. In these processes, diastereomeric salts or complexes of the racemic compounds and resolving agents are formed before the extraction step. The selected resolving agent is added in less than stoichiometric ratio to the racemic compound. The unreacted enantiomers are extracted with the supercritical solvent, and are collected as a powder after depressurization of the solution.

2. Metals recovery using supercritical fluids:

Removal of heavy metals from solid matrices and liquids remain a big challenge and, although various methods have been described for this purpose, SFE seems to be one of the most promising. Complexing agents used in conventional solvent extraction can also be used in SFE complexation of metal ions.

3. SFE in food toxicology and ecotoxicology:

There are several compounds with serious health implications which determination can be done using SFE, the main areas of application include food toxicology and ecotoxicology

4. Solvent removal and new drug delivery formulations:

In order to enhance the bioavailability of poorly water soluble drugs, an increasing number of pharmaceutical formulation technologies are being developed; these include micronization, complex formation and solid dispersions. In the case of polar compounds which are not soluble in supercritical fluids (particularly CO₂), SCFs could be used as antisolvent; in this process, a solution consisting of an organic solvent, completely miscible with the SCF, and a solid material dissolved in this solvent, is

sprayed into a high-pressure vessel filled with SCF. In these processes the supercritical fluid is used to extract the solvent instead of the analyte the spectroscopic and chromatographic characterization of triflusal (2-acetoxy-4- (trifluoromethyl) benzoic acid) delivery systems prepared by using supercritical impregnation technologies. Triflusal is an antithrombogenic drug structurally related to acetylsalicylic acid.

5. Natural pesticides

6. De-nicotinization of tobacco (tar free tobacco)

7. Food preservatives

8. Herbal medicines

9. Pesticides (Neem)

CONCLUSION:

Supercritical fluids have a number of interesting and useful characteristics. Above all, the viewpoints of Noyori et al. in the preceding section are considered to be the most important and interesting. The characteristics of supercritical fluids are that while they form a uniform solution system as a whole, they simultaneously realize a heterogeneous state where the surrounding conditions of the molecules are in constant change with violent fluctuations. Because of such fluctuations, supercritical fluids are a solvent that can realize advantages of both liquid and gas simultaneously.

One of the interesting fields for future research and development would be to make positive studies and use of the fluctuations including solid surfaces, adsorption or heterogeneous catalytic reaction.

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